

of form as the rest of the genus put together, from giant forest trees, to shrubs, herbs, and even geophytes. It is evident that vegetative characters used by previous authors can often provide some indication of the smaller group to which a species belongs, but they are not, on their own, sufficient to identify its relationships positively. In the scheme proposed here (see Fig. 1), characters of the much more stable features of seed, capsule and inflorescence are of prime importance in determining relationships. Habit and vegetative characters of spinescence and branch structure play a secondary role. At the same time they are used as indicators of development within groups, as well as between them, during the gradual adaptation to an arid environment.

Relationships of this very distinct and apparently isolated group of species are not easily determined. Gilbert (1987) has suggested, with some reservation, that it could have been derived from section *Tirucalli* Boiss. (Boissier, 1862). Species of this occur in all the drier regions of Africa, the Arabian Peninsula, and Madagascar, with small leaves quickly deciduous from succulent, cylindrical branches, leaving prominently calloused leaf-scars sometimes surrounded by glandular tissue that could perhaps be homologous with the spine-shield. In personal discussions with Gilbert, it now seems to us that a more likely relationship could lie with a small group of fleshy-stemmed shrubs related to *Euphorbia synadenium* Ridley, from evergreen forests of India and Malaysia. These possess large leaves, with small, persistent stipules, that are leaf-like and often stiffly pointed, resembling the stipular prickles on the spine-shields of tree species in "sub-section *Euphorbia*." This would indicate that subgenus *Euphorbia* (the pair-spined species) may have originated in Asia and migrated to northern Africa at about the time that the continents were breaking up and Madagascar became separated. Development and proliferation within Africa followed as the continent became drier. The relatively few forest species of today retain primitive characteristics, while those of the larger, more successful groups, possessing characters at the most advanced state of adaptation for survival in an arid environment, are found in the extreme habitat conditions of semi-

desert regions, notably in southwest Africa, and especially in the northeast, in the Horn of Africa.

This proposed classification of subgenus *Euphorbia* is based on evidence gained from examination of almost all the species known today. Some gaps remain, especially among the groups with features at the least advanced stage of development and fewer representative species; but these gaps are not great, and it is hoped that, as discoveries of new species are made, they will be filled, and the feasibility of the scheme outlined here will be confirmed.

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PHYTOCHEMISTRY AND SYSTEMATICS OF THE EUPHORBIACEAE¹

David S. Seigler²

ABSTRACT

Phytochemical data provide much useful information concerning relationships both within the Euphorbiaceae and between that family and putative relatives. Within the Euphorbiaceae, the presence of several groups of secondary metabolites support certain infrafamilial groupings, whereas data related to the biosynthesis and distribution of other secondary metabolites provide information concerning the relationship of the Euphorbiaceae to other families. Similarities in chemistry to both the Geraniales and Malvales are found, supporting the suggestion by Webster (1987) that the differences between the Dilliniidae and Rosidae may not be as great as previously thought, and that the Euphorbiaceae may have arisen from ancestors intermediate to those two groups.

The chemistry of the Euphorbiaceae is among the most diverse and interesting of flowering plant families (Evans, 1986a, b; Hegnauer, 1966b, 1989) and is comparable to the biological diversity of the family (Radcliffe-Smith, 1986; Webster, 1987). Because of the presence of unusual secondary metabolites, many species of euphorbiaceous plants are poisonous and have been involved in human and livestock poisoning. Plants of this family, especially those of the genus *Euphorbia*, are known for their ability to induce dermatitis (Evans & Schmidt, 1980). Others have been used in folk medicine, as piscicides, or as arrow poisons. Several euphorbs are important food plants, and a number are important economically as ornamental plants and as sources of rubber, chemical precursors, lubricants, and medicinal compounds (Radcliffe-Smith, 1986; Rizk, 1987).

The principal goal of this article is to evaluate systematic and evolutionary relationships in the Euphorbiaceae with information derived from extant phytochemical literature. These data point to certain affinities of the Euphorbiaceae and suggest alignments of subfamilial taxa of this enigmatic family as well.

What types of secondary compound data are likely to be useful? Both the presence and absence of secondary metabolites and the biosynthetic pathways responsible for their production are useful for establishing taxonomic and phylogenetic relationships. The products of relatively short pathways beginning with readily available precursors are more likely to have originated several times and usually

are widespread among higher plants. Examples are glycosides of the flavones apigenin and luteolin and the flavonols kaempferol and quercetin (Seigler, 1977, 1981b). In general, compounds that are formed via complicated pathways with many steps are less likely to have evolved than those from simple pathways with fewer steps. In deliberations of this sort, one almost must consider the precursors that may be present in a particular plant. Although all diterpenes are of relatively complex biosynthetic origin, many are derived from kaurene, a precursor of gibberellins in plants. Because gibberellins are universal in plants, kaurene, and the biosynthetic pathways leading to kaurene, presumably occur in all plants. Thus, many apparently complex diterpenes actually arise via relatively short modifications of ubiquitous biosynthetic pathways. Examples include compounds such as (-)-kaurene, a diterpene found in several euphorbiaceous taxa.

However, cocarcinogenic diterpenes, found only in the Euphorbiaceae and Thymelaeaceae, are derived from complicated pathways involving numerous steps not shared with other biosynthetic pathways. The probability that the pathways leading to these compounds have evolved more than once is slight, and, hence, the probability that plants that possess these compounds are related is great.

Understanding phylogenetic relationships of the Euphorbiaceae is made difficult by the large number of both morphological and chemical autapomorphic characters. Many exotic and interesting compounds occur in a single species or group of species (Hegnauer, 1989; Rizk, 1987).

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Thousands of compounds from many different chemical classes have been reported from members of the Euphorbiaceae. This article makes no attempt to review the literature exhaustively; references are to recent and readily available review articles rather than to the original works. Readers should consult the references cited in these reviews for more detailed information. A predominance of chemical work concerns the large genus *Euphorbia*, which has been studied in greater detail than most other representatives of the family.

Although the chemistry is doubtful in some instances, a more usual problem involves the uncertain identity of the plant materials used. Voucher specimens were not maintained in many older and some present-day studies. In other instances, the identification of the plant material was not verified by a specialist; this is especially important for the Euphorbiaceae.

MAJOR TYPES OF SECONDARY METABOLITES IN THE EUPHORBIACEAE

Of all chemical classes, the most useful for chemotaxonomic study of the Euphorbiaceae above the level of genus appear to be alkaloids, cyanogenic glycosides, diterpenes, glucosinolates, seed and other lipids, tannins, and triterpenes (Hegnauer, 1966b, 1989). These are useful for several reasons. Alkaloids, diterpenes, tannins, and triterpenes arise from complex pathways; the products have limited distribution within the Euphorbiaceae. Cyanogenic glycosides and glucosinolates arise from pathways of intermediate complexity; although these compounds and the pathways leading to them are found in other plant families, the distribution of these glycosides is restricted within the Euphorbiaceae. Both cyanogenic glycosides and glucosinolates provide useful characters for recognition of subgroups within the family. Other compounds, such as amino acids, coumarins, flavonoids, lignans, monoterpenes, and sesquiterpenes, are widely distributed among many higher plant groups and within the Euphorbiaceae. Although not sufficiently distinctive or restricted in distribution to be useful at the family or subfamily level, these compounds may serve as useful characters at lower taxonomic levels.

ALKALOIDS

Alkaloids are widely distributed in plants. These nitrogenous compounds range from very simple, and usually widespread, to highly complex entities of restricted distribution. Both types are found in the Euphorbiaceae. The use of alkaloids for che-

mosystematic purposes in the Euphorbiaceae previously has been reviewed (Hegnauer, 1963, 1966a, b, 1989; Seigler, 1977).

Among the relatively simple and widespread alkaloids are the harmine types, such as L-3-carboxy-1,2,3,4-tetrahydrocarboline (**1**),³ found in the seeds of *Aleurites fordii* Hemsl. (Crotonoideae: Aleuritidae: Aleuritinae) (Okuda et al., 1975), and *N*_β-methyltetrahydroharman (**2**) isolated from *Spathiostemon javensis* Blume (*Homonoia riparia* (Blume) Müll. Arg.) (Acalyphoideae: Acalyphaeae: Lasiococcinae) (Johns et al., 1970). An ester of vasicine (**3**) (a pyrroloquinazoline alkaloid) has been reported from *Croton draco* Schltdl. (Crotonoideae: Crotonaeae), but some uncertainty exists about the identity of the plant material (Hegnauer, 1966a, b; Rizk, 1987). Several piperidine alkaloids have been reported from members of the Euphorbiaceae. Among these are astrocasine (**4**) [*Astrocasia tremula* (Griseb.) Webster (syn. *Astrocasia phyllanthoides* C. B. Rob. & Millsp.) Phyllanthoideae: Phyllanthaeae: Astrocasinae], 2,4-dimethoxy-Ψ,Ψ-dimethylallyl-*E*-cinnamoylpiperidide (**5**) (*Excoecaria agallocha* L. Euphorbioideae: Hippomaneae: Hippomaninae), and julocrotine (**6**) (*Julocroton* spp.; this genus is only weakly separated from *Croton*) (Rizk, 1987). Hordenine (**7**) is found in *Flueggea virosa* (Willd.) Baill. (syn. *Securinega virosa* (Willd.) Pax & Hoffm.) (Phyllanthoideae: Securineginae) (Hegnauer, 1966b). Pyrrolidine and tropane alkaloids have been reported from *Margaritaria discoideus* (Baill.) Webster (syn. *Phyllanthus discoideus* Müll. Arg.) (Phyllanthoideae: Flueggeinae) (phyllalbine) and *Croton gabouga* S. Moore [4-hydroxyhygrinic acid (**7**)] (Rizk, 1987; Seigler, 1977). An unusual type of quinolizidine alkaloid (**8**) occurs in *Poranthera corymbosa* Brongn. (Phyllanthoideae: Andrachneae: Porantherinae). This series of alkaloids is biosynthetically related to piperidine alkaloids (Howard & Michael, 1986). The hypotensive principle of *Jatropha podagrica* Hook. (Crotonoideae: Jatrophaeae) is tetramethylpyrazine (**9**), a compound also known from members of the Solanaceae and Asclepiadaceae (Nahrstedt, 1982). Purine alkaloids occur in *Cnidioscolus basiacanthus* (Pax & K. Hoffm.) Macbride (syn. *Jatropha basiacantha* Pax & K. Hoffm.) (Rizk, 1987). A questionable report of physostigmine (*Hippomane mancinella* L., Euphorbioideae: Hippomaneae: Hippomaninae) should be confirmed (Lauter & Foote, 1955).

Imidazole alkaloids have been isolated from the

³ See figure at the end of the article.

genera *Glochidion* (Phyllanthoideae: Phyllanthaceae: Flueggeinae) and *Alchornea* (Acalyphoideae: Alchorneae: Alchorneinae) (Johns & Lambert, 1967; Maat & Beyerman, 1983; Rizk, 1987). A series of imidazole alkaloids including N^{α} -cinnamoylhistamine (**15**), N^{α} -oxodecanoylhistamine (**10**), glochidicine (**11**), and glochidine (**12**) occur in *Glochidion philippicum* (Cav.) C. B. Rob. (Rizk, 1987). Alkaloids with this general structure are known from several other groups of plants (Acanthaceae, Cactaceae, Fabaceae, Orchidaceae, and Rutaceae), but the structures are so diverse that the alkaloids may be of distinct biosynthetic origin (Seigler, 1977).

The pyrimidine and guanidine alkaloids of *Alchornea* contain a hemiterpene unit and also represent an unusual structural type. Among the pyrimidine alkaloids of *Alchornea javanensis* Müll. Arg. are alchornidine (**13**) and alchornine (**14**). This plant also contains N^1, N^2 -diisopentenylguanidine and N^1, N^2, N^3 -triisopentenylguanidine (Hegnauer, 1989; Rizk, 1987).

Because of the widespread occurrence of the above alkaloids among other plants (probably reflecting the ease with which they can arise), and/or their sporadic distribution among the Euphorbiaceae, their presence does not suggest or confirm familial or subfamilial relationships. However, other genera related to *Glochidion* and *Alchornea* should be examined for the presence of imidazole, pyrimidine and guanidine alkaloids, respectively, as these compounds could provide useful characters at the specific and generic level.

In contrast, the distribution of benzyloquinoline alkaloids is restricted among higher plants. Most occur in certain families of the Magnoliales and Ranunculales, although sporadic occurrences are known from other plant groups. Benzyloquinoline alkaloids are common in the following families: Annonaceae, Aristolochiaceae, Berberidaceae, Eupomatiaceae, Hernandiaceae, Fumariaceae, Lauraceae, Magnoliaceae, Menispermaceae, Monimiaceae, Nelumbonaceae, Papaveraceae, Ranunculaceae, and Winteraceae. Alkaloids of this structural type are found less commonly in other families including the Euphorbiaceae (*Croton*, *Andrachne*), Fabaceae (*Erythrina*), Rhamnaceae (*Rhamnus*, *Phylla*, *Colletia*, *Colubrina*, *Discaria*, *Ratanilla*, *Talguenea*, and *Zizyphus*), Phellinaceae (*Phellina*), Symplocaceae (*Symplocos*), Rutaceae, Araliaceae (*Hedera*), Apiaceae (*Heraclium*), Caprifoliaceae (*Symphoricarpos*), Rubiaceae (*Cephaelis*), and Araceae (*Lysichiton*) (Bisset, 1985; Dahlgren et al., 1981).

In the Euphorbiaceae, aporphine (thaliporphine

and glaucine), proaporphine, dihydroproaporphine, and morphinandienone types of benzyloquinoline alkaloids have been isolated from *Croton* species (Rizk, 1987; Rizk & El-Missiry, 1986). Among the individual alkaloids isolated are glaucine (**16**), orotonsine, pronuciforine, sparsiflorine (**17**), thaliporphine, crotsparine (**18**), *N,O*-crotsparine, *N*-methylcrotsparine, crotonosine (**19**), flavinantine, flavinine, linearisine (**20**), 3-methoxy-4,6-dihydroymorphinandien-7-one, *N*-norsalutaridine, norsinoacutine, salutaridine (**21**), and salutarine (Rizk, 1987). Salutaridine was first discovered in *Croton salutaris* Casar. from Brazil and later found in low concentrations in *Papaver somniferum* L., where it is an intermediate in the biosynthesis of morphine alkaloids. Bisbenzyloquinoline alkaloids have been reported from *Andrachne cordifolia* (Decne.) Müll. Arg. (Phyllanthoideae: Andrachneae: Andrachninae) (Khan et al., 1983).

The securinine alkaloids are a small group of compounds produced only by members of the subfamily Phyllanthoideae. Among these, allosecurinine (**22**), dihydrosecurinine, norsecurinine (**23**), phyllantidine, phyllantine, phyllochrysinine, securinine (**24**), suffruticosine, and virosecurinine (**25**) come from *Securinega*, *Phyllanthus*, and *Flueggea* (Phyllanthaceae: Flueggeinae) species. Securinine and related alkaloids are synthesized from lysine and tyrosine via a unique pathway and represent a novel type of alkaloids not found in other plant groups (Beutler & Brubaker, 1987; Rizk, 1987; Seigler, 1977). Their presence in several members of the Phyllanthoideae reinforces the close relationship of the genera *Phyllanthus*, *Flueggea*, and *Securinega*.

Ricinine (**26**) (*Ricinus communis* L., Acalyphoideae: Acalypheae: Ricininae), nudiflorine (**27**), ricinidine (**28**), methyl-3-carboxamide-6-pyridone (*Trewia* spp., Acalyphoideae), and mallorepine (**29**) (*Mallotus*, Acalyphoideae; Acalypheae: Rottleriinae) all appear to be closely related and are probably derived from nicotinic acid (Fodor & Colosanti, 1985; Sastry & Waller, 1972; Strunz & Findlay, 1985; Waller & Nowacki, 1978). The structures of these alkaloids suggest a similar biosynthetic origin from nicotinic acid as is probably true for the cyanogenic glycoside acalyphin (**30**) (*Acalypha indica* L., Acalyphoideae: Acalypheae: Acalyphinae) (Nahrstedt, 1987).

Maytansinoid alkaloids, such as trewiasine (**31**) are reported often from plants of the genera *Maytenus* and *Putterlickia* of the Celastraceae and *Colubrina* of the Rhamnaceae (Reider & Roland, 1984), but also have been encountered in the genus *Trewia* (Powell et al., 1981, 1983).

Peptide alkaloids are known from *Hymenocardia acida* Tul. (Phyllanthoideae: Hymenocardieae) (Pais et al., 1967; Seigler, 1977). Similar alkaloids, such as hymenocardine (**32**) have been isolated from *Panda* of the Pandaceae, which Webster (1994) now merges with the Euphorbiaceae. This merger is supported by peptide alkaloid chemical data. Peptide alkaloids also have been isolated from the Celastraceae, Menispermaceae (*Cocculus*), Rhamnaceae, Rubiaceae, Sterculiaceae (*Melochia* and *Waltheria*), and Urticaceae (Schmidt et al., 1985).

CYANOGENIC GLYCOSIDES

Plants from subfamilies Phyllanthoideae, Crotonoideae, and Acalyphoideae of the Euphorbiaceae contain glycosides capable of releasing cyanide upon hydrolysis. This property also has been reported, but not confirmed, from plants of the Euphorbioideae. The cyanogenic glycosides involved are derived from several different precursors, and although one compound of this type, acalyphin (**30**), is found only in the Euphorbiaceae, others are widely distributed.

Several species of the subfamily Phyllanthoideae are cyanogenic. Among these are *Andrachne colchica* W. Fisch. & E. Meyer*, *A. decaisnei* Benth., *A. telephioides* L.*, *Breynia obtusiflora*, *Bridelia cathartica* G. Bertol. *, *B. exaltata* F. Muell., *B. duvigneaudii* J. Léonard, *B. mollis* Hutch., *B. monoica* Merr.*, *B. ovata* Decne., *B. pervilleana* Baill., *B. scleroneura* Müll. Arg.*, *B. tomentosa* Blume, *Phyllanthus acuminatus* Vahl., *P. angustifolius* (Sw.) Sw., *P. gasstroemii* Müll. Arg., *P. lacunarius* F. Muell., *P. speciosus* Jacq., *Poranthera microphylla* Brongn.*, *P. corymbosa*, *Flueggea suffruticosa* (Pall.) Baill.* [syn. *Securinea suffruticosa* (Pall.) Rehder, *S. ramiflora* Müll. Arg., and *S. flueggeoides* Müll. Arg.] (van Valen, 1978). Those species marked with an * are known to contain triglochinin (**33**) as the cyanogenic glycoside; other species are known to be cyanogenic, but the compounds have not been characterized. Plants of *Phyllanthus gasstroemii* contain taxiphyllin (**34**). Plants of *Bridelia monoica* contain dhurrin (an enantiomer of taxiphyllin) and triglochinin (Hegnauer, 1989; van Valen, 1978), but no other cyanogens have been substantiated from species of this subfamily (Brideliaceae). All three cyanogens are derived from tyrosine.

A number of species of the subfamily Crotonoideae are known to be cyanogenic. Among these are *Aleurites trisperma* Blanco, *Beyeria lesche-*

naultii (DC.) Baill. and *B. viscosa* (Labill.) Miq. (Ricinocarpeae: Ricinocarpinae), several species of *Cnidoscolus*‡ (Manihoteae), *Croton lobatus* L., *C. punctatus* Lour., *C. scouleri* Hook. f., *Elatiospermum tapos* Blume (Elatiospermeae), several *Hevea*‡ species (Micrandreae: Heveinae), many species of *Manihot* (*Manihot esculenta* Crantz‡) (Manihoteae), (Adsersen et al., 1987; Hegnauer, 1989; van Valen, 1978). Weakly positive tests have been observed with some species of the genus *Jatropha* (e.g., *J. capensis* Sond.). Most of the species examined in this subfamily contain linamarin (**35**) and usually smaller amounts of lotaustralin (**36**) (species marked with a ‡). In addition, careful examination of the cyanogens of *Hevea brasiliensis* Müll. Arg. (Crotonoideae: Micrandreae: Heveinae) revealed the presence of the corresponding diglycoside, linustatin (**37**) (Lieberei, 1986, 1988). In general, lines of *Hevea brasiliensis* with large amounts of cyanogenic glycosides and β -glycosidases are the most susceptible to the South American leaf blight (Lieberei, 1988). Cyanogenic diglycosides, such as linustatin, appear to be involved in transport of cyanogenic glycosides within the plants and are probably more widely distributed than realized (Lieberei et al., 1985).

Several species from the Acalyphoideae also are known to be cyanogenic. Among these are *Acalypha indica* L., *A. ostryaefolia* Riddell, *Dalechampia micromeria* Baill. (Plukenetieae: Dalechampiinae), *Mercurialis annua* L. (Acalyphaceae: Mercurialinae), and *Ricinus communis* (Hegnauer, 1989; Nahrstedt, 1987; van Valen, 1978). The cyanogenic glycoside acalyphin (**30**) has been isolated from *Acalypha indica* (Nahrstedt, 1987).

A number of plants of the subfamily Euphorbioideae have been reported to be cyanogenic. Among these are *Chamaesyce abdita* Burch, *C. galapageia* (B. L. Rob. & Greenm.) Burch, *C. hirta* (L.) Millsp. (*Euphorbia hirta* L.), *C. maculata* (L.) Small [*C. supina* (Raf.) Moldenke], *C. recurva* (Hook. f.) Burch, *C. thymifolia* (L.) Millsp. (*Euphorbia thymifolia* L.), *C. viminea* (Hook. f.) Burch (Euphorbieae: Euphorbiinae), *Euphorbia drummondii* Boiss. [probably *E. boophthona* C. A. Gardner and *E. clutioides* (G. Forst.) C. A. Gardner], *E. eylesii* Rendle, *E. hexagona* Nutt., *E. lupatensis* N. E. Br. (Euphorbieae: Euphorbiinae), *Gymnanthes lucida* Sw. (Hippomaneae: Hippomaninae), *Sapium haemospermum* Müll. Arg., *S. sebiferum* (L.) Roxb. (Hippomaneae: Hippomaninae), *Stillingia dentata* (Torr.) Britton & Rusby, *S. sanguinolenta* Müll. Arg. (Hippomaneae: Hippomaninae), and doubtfully *Colliguaja integerrima* Gillies & Hook. (Hippomaneae: Hip-

pomaninae) (Hegnauer, 1989). To date, the cyanogenic compounds of the Euphorbioideae have not been characterized.

DITERPENES

A large variety of diterpenes occur in the Euphorbiaceae (Hegnauer, 1966b, 1989). These may be grouped into compounds derived from monocyclic precursors and their derivatives (including cocarcinogenic diterpenes), kaurene and related compounds, and labdane derivatives.

Simple diterpenes from geranylgeranyl pyrophosphate. Geranylgeraniol derivatives are found in several species of *Croton*, e.g., *C. kerrii* Airy Shaw and *C. sublyratus* Kurz. (Hegnauer, 1989). One simple diterpene, 18-hydroxy-6-*cis*-geranylgeraniol (**38**) from *Croton kerrii* stems, appears to serve as a prostaglandin analogue. This compound protects the digestive tract from the effects of ulceration and promotes wound healing (Croteau & Johnson, 1985; Sato et al., 1980).

Cyclic diterpenes from geranylgeranyl pyrophosphate. Cembrene (**39**), duvatrienediols (such as **40**), and a large series of compounds of the Euphorbiaceae (the lathyrols, casbene, jatrophanes, rhamnifolanes, and crotofolanes, as well as the cocarcinogenic tiglianes, daphnanes, and ingenanes) are derived from cyclization of a geranylgeranyl pyrophosphate precursor to a large monocyclic system (Schmidt, 1987). Casbene (**41**), a bicyclic 14-membered ring compound, is a phytoalexin in *Ricinus communis*. This compound appears to be derived from head-to-tail condensation of the diterpene pyrophosphate precursor, geranylgeranyl pyrophosphate (GGPP) (Schmidt, 1987). A compound with related structure has been isolated from *Croton nitens* Sw.

Several unusual structural types of diterpenes derived from monocyclic precursors occur in the Euphorbiaceae. Jatrophanes (such as **42**) are known from *Jatropha gossypifolia* L., *J. macrorhiza* Benth., *Euphorbia characias* L., *Euphorbia esula* L., *E. maddenii* Boiss., *E. helioscopia* L., and *E. kansui* Liou ex H. B. Ho (Hegnauer, 1989; Manners, 1987; Schmidt, 1987). Rhamnifolanes (**43**) are known from *Croton rhamnifolius* Kunth. (Schmidt, 1987). Lathyranes (such as **44**) are known from *Bertya cupressoidea* Airy Shaw (Crotonoideae: Ricinocarpeae: Bertyinae), *Euphorbia helioscopia* L., *Euphorbia characias*, *E. ingens* E. Meyer, *E. jolkini* Boiss., *E. lathyris* L., and *Macaranga tanarius* Müll. Arg. (Acalyphoideae: Acalypheae: Macaranginae) (Hegnauer, 1989; Schmidt, 1987). Crotofolanes (such as **45**) are

known from *Croton corylifolius* Lam. (Schmidt, 1987).

Cocarcinogenic diterpenes. The powerful purgative properties of "croton oil," the seed oil of *Croton tiglium* L. (native to Southeast Asia), have long been known. The active compounds have been isolated and shown to consist of the 12,13-diesters of a tetracyclic diterpene, phorbol (**46**) (Hecker & Schmidt, 1974). These compounds are potent irritants and cocarcinogens (Evans & Schmidt, 1980; Evans & Soper, 1978; Hecker, 1977, 1986; Kinghorn, 1979). These compounds are called cocarcinogens or tumor promoters because they are not directly carcinogenic, but application of a carcinogen following contact with cocarcinogenic diterpenes results in greatly enhanced carcinogenic activity. At the same time, these compounds have been examined for their antitumor properties (Evans & Soper, 1978; Hecker, 1986).

Biosynthetically, these compounds are derived from monocyclic diterpenoid precursors and are biosynthetically related to casbene, the lathyranes, and the jatrophanes. Several major structural types are found. Most important among these types are the ingenane (such as **47**) (Schmidt, 1986b), daphnane (**48**) (Schmidt, 1986a), and tigliane (**46**) (Evans, 1986a, b) series. Precursors of the tiglianes, ingenanes, and daphnane type cocarcinogenic diterpenes have been isolated from the Euphorbiaceae as well as Thymelaeaceae.

Tiglianes (e.g., phorbol) (tetracyclic with a six- and a seven-membered ring) occur in *Aquilaria*, *Daphnopsis*, *Pimelea* (Thymelaeaceae) as well as *Aleurites*, *Croton* (Crotonoideae), *Euphorbia*, *Hippomane*, *Sapium*, and *Synadenium* (Euphorbioideae: Euphorbieae: Euphorbiinae) (Bagavathi et al., 1988; Hecker, 1977; Evans & Soper, 1978; Schmidt, 1986c).

Ingenanes (e.g., ingenol) (tetracyclic with two seven-membered rings) occur in *Euphorbia* (and *Elaeophorbia*, considered a synonym of *Euphorbia* by Webster, 1975, 1994) species (Hecker, 1977; Evans & Soper, 1978), but not in other taxa of the Euphorbiaceae and Thymelaeaceae that were examined (Hecker, 1977).

Daphnane compounds (e.g., daphnetoxin) (tricyclic) occur in both the Euphorbiaceae [*Baliospermum* (Crotonoideae: Codiaeae), *Cunuria* (Crotonoideae: Micrandreae: Micrandrinae), *Euphorbia*, *Excoecaria*, *Hippomane*, *Hura* (Euphorbioideae: Hureae), and *Stillingia*] and the Thymelaeaceae (*Daphne*, *Daphnopsis*, *Diarthron*, *Dirca*, *Gnidia*, *Lasiosiphon*, *Pimelea*, *Synaptolepis*, *Thymelaea*,

and *Wikstroemia*) (Adolf et al., 1988; Hecker, 1977; Powell et al., 1985; Schmidt, 1986c). Daphnanes are probably derived from tiglanes by opening of the cyclopropane ring (Evans & Soper, 1978).

Within the genus *Euphorbia*, subgenera *Chamaesyce* and *Poinsettia* lack cocarcinogenic diterpenes. Both tiglanes and ingenanes are common in subgenera *Euphorbia* and *Tithymalus* (Evans & Kinghorn, 1977; Evans & Soper, 1978).

Determination of active diterpenes by means of a 3H-PDBU (tritiated phorbol receptor binding assay) suggested their presence in several previously untested samples of euphorbiaceous plants. Activity was observed in the Phyllanthoideae [*Antidesma* (Antidesmeae: Antidesminae), *Drypetes* (Drypeteae), *Glochidion*, and *Uapaca* (Uapaceae)], although only that observed in *Antidesma* was strongly positive (Beutler et al., 1989). Cleistanthol, a cocarcinogenic diterpene, is found in *Cleistanthus schlechteri* Hutch. (Phyllanthoideae: Brideliaceae) (McGarry et al., 1971). Only weak activity was observed in the Acalyphoideae (*Alchornea* and *Trewia*) and none from the Oldfieldioideae. Among the Crotonoideae, activity was found in *Cnidioscolus*, *Jatropha*, *Ricinodendron* (Aleuritidae: Ricinodendrinae), *Codiaeum*, *Dimorphocalyx*, *Fahrenheitia* (Codiaeae), *Aleurites*, *Crotonogyne* (Neoboutonieae: Crotonogyninae), *Cyrtogonone* (Neoboutonieae: Crotonogyninae), *Croton* (including *Eremocarpus*) (Crotonae) (Beutler et al., 1989). Similar activity was observed in *Aleurites fordii* (Aleuritidae: Aleuritinae) (Schmidt, 1987). In the Euphorbioideae, activity was found in *Plagiostyles* (Stomatocalyceae: Stomatocalycinae), *Homalanthus* (Hippomaneae: Carumbiinae), *Duvigneaudia* (Hippomaneae: Hippomaninae), *Excoecaria*, *Hippomane*, *Maprounea* (Hippomaneae: Hippomaninae), *Sapium*, and *Stillingia* (Beutler et al., 1989). A large number of other genera were examined and found to lack this activity.

Diterpenes derived from kaurene. Kaurene (49) is probably found in all plants as it is a precursor for gibberellins, although usually only in small amounts. Structurally related compounds are accumulated in a number of euphorbiaceous taxa. For example, *ent-3 β -hydroxybeyer-15(16)-ene-2,12-dione* (50) is known from *Androstachys johnsonii* Prain (Oldfieldioideae: Picrodendreae: Androstachydeae) (Pegel et al., 1971), *Beyeria leschenaultii* (DC.) Baill., and *B. calycina* Airy Shaw (Bakker et al., 1972; Ghisalberti et al., 1978). Many pimarane and abietane derivatives are

found in the Asteraceae, Lamiaceae, Euphorbiaceae, and the genus *Jungermannia* (a bryophyte) (Croteau & Johnson, 1985). These compounds occur in the leaf-surface resins of members of the tribe Ricinocarpoideae (Croteau & Johnson, 1985; Dell & McComb, 1974).

Oxygenated diterpene derivatives. A number of highly oxygenated diterpenes based on the labdane skeleton are found in the families Asteraceae, Euphorbiaceae, Lamiaceae, and Verbenaceae (Croteau & Johnson, 1985; Seigler, 1981a). These compounds are complex and restricted in distribution. In the Euphorbiaceae, they are primarily found in the genus *Croton* (Seigler, 1981a). Furan formation between C-15 and C-16 is common. Such compounds are cordylifoline (Burke et al., 1976) and isocrotocaudin (51). At least two diterpenes of this type are found in *Croton setigerus* Hook. [*Eremocarpus setigerus* (Hook.) Benth.] (Bajaj et al., 1986; Jolad et al., 1982), and another compound, mallotucin A, isolated from *Mallotus repandus* (Willd.) Müll. Arg. has been shown identical to teucrin (52) [originally isolated from *Teucrium* (Lamiaceae)] (Kawashima et al., 1976).

GLUCOSINOLATES

Glucosinolates in the Euphorbiaceae are confined to a small number of taxa. Most important among these are *Drypetes gossweileri* S. Moore and *Putranjiva roxburghii* Wall. (Phyllanthoideae: Drypeteae). *Putranjiva* is merged with *Drypetes* by some (Hurusawa, 1954). Glucoputranjivin (53), glucocochlearin (54), and glucojaputin have been isolated from *Putranjiva roxburghii* (Rizk, 1987). Although glucosinolates are derived from the same pathways as cyanogenic glycosides, glucosinolates of the Euphorbiaceae are based on aliphatic aglycones and do not resemble the cyanogenic glycosides of this subfamily. Benzyl isothiocyanate has been reported from the latex of *Jatropha multifida* L. (Rizk & El-Missiry, 1986).

Among higher plants, the distribution of glucosinolates is restricted to a small number of families (Rodman, 1991a, b; Rodman et al., 1993). One group of families includes the Brassicaceae, Capparidaceae, Resedaceae, and Tovariaceae. A number of other enigmatic glucosinolate-containing families appear to be related to those families. Several other glucosinolate-containing families may be related to each other, but the glucosinolate-containing members of the Euphorbiaceae do not appear to be closely related to any other glucosinolate-containing plants (Hegnauer, 1966b; Rodman, 1991a, b; Rodman et al., 1993).

SEED AND OTHER LIPIDS

A number of unusual fatty acids occur primarily as components of seed lipids of members of the Euphorbiaceae but are occasionally found in the lipids associated with other plant parts (Smith, 1970). Many of these involve unusual sites of unsaturation and *E* double bonds. For example, *Sapium sebiferum* (L.) Roxb. contains decanoic acid with 2-*E*-4-*Z* unsaturation (55) and *Sebastiania ligustrina* (Michx.) Müll. Arg. contains dodeca-2,4-dienoic acid (56) (Smith, 1970). A decanoic acid with a cyclopropane ring (57) has been isolated from *Croton* species (Hegnauer, 1989).

α -Eleostearic acid (58) is found in tung oil (*Aleurites fordii*, *A. montana* (Lour.) E. H. Wilson, *A. remyi* Sherff., and *A. trisperma*, but only questionably from the seed oil of *A. moluccana* Willd.). This rapidly polymerizing acid is also found in the oil of *Garcia nutans* Rohr., *Ricinodendron viticoides* Mildbr., and *R. rautanenii* Schinz. (Crotonoideae: Aleuritidae: Ricinodendrinae), (Hegnauer, 1989; Jacobson et al., 1981; Smith, 1970).

An unusual glyceride containing an allenic linkage and a short chain hydroxy acid (59) is found in the seed lipids of *Sapium sebiferum*, *Stillingia sylvatica* L., *Stillingia texana* I. M. Johnst., and *Sebastiania ligustrina* (Michx.) Müll. Arg. (Hegnauer, 1989; Heimermann & Holman, 1972).

Various hydroxy acids also occur. Although found in other plants and microorganisms (for example, in fungi of the genus *Claviceps*), ricinoleic acid (60) is the major fatty acid of the triglycerides of *Ricinus communis*. *Securinega suffruticosa* seed oil contains 12-hydroxyheptadecanoic (61) and 12-hydroxyeicosanoic acids (Hegnauer, 1989). The main constituent of the seed oil of *Mallotus philippensis* (Lam.) Müll. Arg. and *Trewia nudiflora* L. is 18-hydroxyoctadec-*Z*-9-*E*-11-*E*-13-trienoic (α -kamolenic) acid (62) (Calderwood & Gunstone, 1953; Hegnauer, 1989).

Epoxy fatty acids are found in *Alchornea cordifolia* Müll. Arg. [a rich source of (+)-*Z*-14,15-epoxy-*Z*-11-eicosenoic acid (63)] (Kleiman et al., 1977), *Cephalocroton cordofanus* Hochst. (Acalyphoideae: Epiprineae: Epiprinineae) (Bharucha & Gunstone, 1956), and *Euphorbia lagascae* Spreng. (vernolic or *cis*-12,13-epoxyoleic acid) (64) (Kleiman et al., 1965; Smith, 1970). The furanoid compound, 10,13-epoxy-11-methyloctadeca-10,12-dienoic acid (65), occurs in the latex of *Hevea brasiliensis* (A. Juss.) Müll. Arg. (Hasma & Subramaniam, 1978).

Dihydroxy fatty acids are found commonly in the Euphorbiaceae as well as in several other families. These compounds are thought to be derived

biosynthetically from epoxy fatty acids. 9,14-dihydroxyoctadecadien-10,12-oic acid (67) and *erythro*-9,10-dihydroxy-1-octadecanyl acetate (66) are found in the seeds of *Aleurites fordii* and 11,13-dihydroxy-9-*trans*-tetracosenoic acid in *Baliospermum axillare* Blume (Hegnauer, 1989).

TANNINS

Polyphenolic compounds known as tannins are especially widespread among woody plants, but also are found in herbaceous species. Both hydrolyzable and condensed tannins are found in plants from the Euphorbiaceae (Rizk & El-Missiry, 1986). Hydrolyzable tannins that yield ellagic acid (68) on hydrolysis have been reported from several species, primarily from the genus *Euphorbia* (Rizk & El-Missiry, 1986). One specific ellagitannin, geraniin (69), is widespread in the family and has been isolated from members of the Acalyphoideae, Crotonoideae, Euphorbioideae, and Phyllanthoideae (Hegnauer, 1989; Okuda et al., 1980). In the first three of these subfamilies, it is accompanied by the rarely encountered compound mallotusic acid (70). Geraniin is especially common in the Geraniaceae, but absent from the Myrtaceae, Fagaceae, and Fabaceae. Tannins with quite distinctive structures have been isolated from euphorbiaceous plants, especially from the genus *Euphorbia* (Okuda et al., 1980).

Because tannins have complex structures and in some cases appear to have restricted distribution, these compounds should be useful for systematic studies. Unfortunately, tannins occur in complex mixtures; this complexity has precluded analysis in many cases. Tannin content alone is not useful for taxonomic purposes. Future work may clarify the structures of many of these compounds and provide additional chemosystematic markers for analysis of plant groups.

TRITERPENES

Many plants of the Euphorbiaceae possess latex that is rich in terpenes. Triterpenes are predominant in these terpenoid fractions in most species. Reviews of triterpenes (Das & Mahato, 1983; Hegnauer, 1989; Ourisson et al., 1979; Pant & Rastogi, 1979; Rizk & El-Missiry, 1986; Seigler, 1981a) include many references to the Euphorbiaceae. Species of triterpenes from the genus *Euphorbia* easily outnumber those of all other euphorbiaceous taxa (Hegnauer, 1989; Ourisson et al., 1979; Ponsinet et al., 1968; Ponsinet & Ourisson, 1965).

Most of the triterpenes that have been reported from the Euphorbiaceae (e.g., β -sitosterol, α - and β -amyrin (71), friedelan, taraxerol, lupeol (72),

cycloartenol (73), taraxerone, β -amyirin acetate, pseudotaraxasterol, betulin, taraxerone, 24-methylenecycloartenol, taraxasterol, friedilin, oleanolic acid, and butyrospermol) are widespread among higher plants and are of little value for establishing taxonomic relationships at higher levels. Their presence may, however, be useful taxonomically at the species or subgeneric level (Mahlberg et al., 1988). Because triterpenes are difficult to isolate, purify, and characterize, many older reports (for example, those for lanosterol) should be re-examined.

Euphol (74), tirucallol (75), and euphorbol (76) often are found in the latex of members of the genus *Euphorbia* (Rizk & El-Missiry, 1986). In addition, euphol is found in the Burseraceae, Rutaceae, Simaroubaceae, Cneoraceae, and Meliaceae, and tirucallol in the Anacardiaceae; either (or both) serve as precursors for a series of metabolically altered triterpenes in the Cneoraceae, Meliaceae, Rutaceae, and Simaroubaceae.

Hundreds of *Euphorbia* species have been examined for triterpene content. The major triterpenes present are compounds related to cycloartenol, tetracyclic triterpenes, and pentacyclic triterpenes (Hegnauer, 1989; Ourisson et al., 1979). Bauerenol (77), germanicol (78), and phyllanthol (79) are pentacyclic triterpenes found in many plants from the genus *Euphorbia* (Rizk & El-Missiry, 1986). In general, herbaceous species accumulate cycloartenol, cactuslike species accumulate euphol and euphorbol, whereas "coral-like species" accumulate euphol and tirucallol (Ponsinet et al., 1968; Ourisson et al., 1979; Ramaiah et al., 1979; Rizk & El-Missiry, 1986). Members of the American subgenus *Poinsettia* usually contain fatty acid esters of pentacyclic triterpenes (Hegnauer, 1989; Ourisson et al., 1979). Although cholesterol is normally a minor plant sterol, in *Euphorbia pulcherrima* Willd. this compound comprises almost half the sterol mixture (Rizk & El-Missiry, 1986).

There have been too few other investigations to apply the data effectively, but probably plants of most other euphorbiaceous genera do not accumulate triterpenes to the same extent as do species of *Euphorbia*.

A number of new and distinctive compounds (primarily pentacyclic triterpenes related to lupeol) have been reported from the genus *Glochidion* (Hegnauer, 1989; Rizk & El-Missiry, 1986).

Cardiac glycosides (such as 80), another group of triterpenoid derived compounds sporadically distributed among plants, are found in several members of the genus *Mallotus* (Rizk, 1987; Roberts et al., 1966).

Cucurbitacins (such as 81) have been reported from the Phyllanthoideae [*Antidesma rupicola* Wedd., *Cleistanthus rupicola* J. Léonard, *Drypetes gossweileri*, *Spondianthus preussii* Engl. (Antidesmeae: Spondianthinae)], the Acalyphoideae [*Discoglyprena coloneura* Prain. (Caryodendreae), *Mareya micrantha* (Benth.) Müll. Arg. (Acalypheae: Claoxylinae), *Trewia nudiflora*], and the Euphorbioideae (*Maprounea africana* Müll. Arg., *Sapium cornutum* Pax) (Hegnauer, 1989). These extremely bitter compounds also occur in the Cucurbitaceae, Brassicaceae (*Iberis*), Liliaceae (*Phormium*), Begoniaceae (*Begonia*), Rosaceae (*Purshia*), Datisceae, Sterculiaceae (*Helicteres*), Scrophulariaceae (*Gratiola*), Polemoniaceae (*Ipomopsis*), and Primulaceae (*Anagallis*).

MISCELLANEOUS COMPOUNDS

Amino acids. 3,4-Dihydroxy-L-phenylalanine (L-dopa) (82), a nonprotein amino acid, is used for treatment of Parkinson's disease. This compound is found in several plants, primarily legumes, but also occurs in *Euphorbia lathyris* L. (Hegnauer, 1966b).

Coumarins. Many coumarins are essentially ubiquitous in higher plants. Compounds such as umbelliferone, esculin, esculetin, scopolin, scopoletin, and coumarin occur in many plant families. The bicoumarins euphorbetin and isoeuphorbetin are found in *Euphorbia lathyris* (Euphorbioideae) (Rizk, 1987). Bergenin (83) derivatives are found in the bark of *Mallotus japonicus* Müll. Arg., *Mallotus repandus*, and *Macaranga peltata* Müll. Arg. (Acalyphoideae) and in *Flueggea microcarpa* Blume (Ramaiah et al., 1979; Rizk, 1987). Bergenin frequently accompanies ellagitannins in euphorbiaceous plants (Hegnauer, 1989). Benzocoumarins have been isolated from *Euphorbia royleana* Boiss. (Rizk, 1987).

Flavonoids. Flavonoids are ubiquitous components of plants. Several types, such as the glycosides of the flavones apigenin and luteolin, and the flavonols kaempferol and quercetin are found in a large percentage of plants examined. Other types of flavonoids, such as biflavonoids, are less widely distributed.

Numerous flavonoids have been isolated and characterized from members of the Euphorbiaceae (Rizk, 1987; Rizk & El-Missiry, 1986). Both C- and O-glycosides are found. Many compounds, such as quercetin and quercetin glycosides (e.g., isoquercitrin (84)), rutin, vitexin (85), isovitexin, isorhamnetin, orientin, isoorientin, kaempferol and kaempferol glycosides, rhamnetin, naringen gly-

cosides, apigenin and apigenin glycosides, quercitrin, isoquercitrin, and saponarin, as well as the anthocyanidins cyanidin, delphinidin, and pelargonidin are widespread within the Euphorbiaceae and also are found in many other plant families. Although the distribution of these glycosides might be useful for study of problems at lower hierarchical levels, most flavonoids are not particularly useful for study of relationships at higher taxonomic levels.

The presence of other, more unusual types of flavonoids has more promise in this regard. For example, 8-methoxyflavonoids [e.g., gossypetin (86)] are found in several taxa of the tribe Ricinocarpeae (subfamily Crotonoideae), including *Beyeria brevifolia* Baill., *B. leschenaultii*, *Ricinocarpos muricatus* Müll. Arg., and *R. stylosus* Diels (Rizk & El-Missiry, 1986).

Biflavonoids (e.g., heveaflavone (87)) are found in a number of families, including the Pinaceae, Anacardiaceae, Casuarinaceae, Clusiaceae, Ochnaceae, Rhamnaceae, Caprifoliaceae, and Euphorbiaceae (Geiger & Quinn, 1982). These compounds are also found in certain mosses, cycads, and in *Ginkgo biloba* L.

Hydrocarbons and waxy materials. Because many euphorbiaceous plants occur in deserts and dry areas, they have thick cuticles and a relatively large amount of waxy material (Gnecco et al., 1989; Rizk & El-Missiry, 1986). Most of the long chain hydrocarbons, alcohols, aldehydes, acids, and wax esters of the Euphorbiaceae are similar to those of other plant groups.

Candelilla wax of *Euphorbia antisiphilitica* Zucc., and the waxes of *E. cerifera* Alcocer, *Pedilanthus cymbiferus* Schldl. (syn. *Pedilanthus aphyllus* Boiss.), and *Pedilanthus bracteatus* (Jacq.) Boiss. (syn. *Pedilanthus pavonis* Bois.) (Euphorbioideae: Euphorbieae: Euphorbiinae) are commonly used in cosmetics and as an extender in other wax products (Rizk, 1987; Schery, 1972). Candelilla wax is comprised of both hydrocarbon fractions and wax esters.

Monoterpenes. Monoterpenes are ubiquitous among plants. Few of the structures are so characteristic as to be useful in a chemosystematic sense with problems above the species level. Accumulation of monoterpenes as a class is common in the genus *Croton*, *Croton setigera* (*Eremocarpus setigerus*), and *Joannesia princeps* Vell. (Crotonoideae: Joannesieae) (Farnsworth et al., 1969; Hegnauer, 1966b, 1989). Few other taxa in the family accumulate significant quantities of these compounds in vegetative portions of the plant, although

they are involved in attraction of pollinators in several taxa (e.g., *Dalechampia*).

Proteins and peptides. The seeds of several members of the Euphorbiaceae contain toxic proteins. For example, the castor bean, *Ricinus communis*, contains antigenic proteins that agglutinate defibrinated blood and red blood cells in vitro. As few as two to four seeds of this plant can be lethal, and eight are almost always lethal (Kingsbury, 1964). Ricin is a dimeric protein with two different peptide chains (MW 63,000). The seeds of *Aleurites fordii*, *Jatropha curcas* L., and *J. multifida* L. also produce toxic proteins that have not been studied extensively.

Rubber. Among the Euphorbiaceae, latex is found primarily in members of the subfamilies Crotonoideae and Euphorbioideae but generally is lacking in the Phyllanthoideae, Oldfieldioideae, and Acalyphoideae (Hegnauer, 1966b, 1989). Although latex is a complex mixture of diterpenes, triterpenes, enzymes, amino acids, and other components, polymeric isoprenoid compounds are important in most. Several plants of the Euphorbiaceae produce all *cis*-polyisoprene (natural rubber). Best known among these is *Hevea brasiliensis*, but similar materials are produced by other *Hevea* species, *Manihot glaziovii* Müll. Arg. (ceara or manicobe rubber), *Micrandra* species (Crotonoideae: Micrandreae: Micrandrinae) (caura rubber), and *Cnidioscolus* species (chilte rubber) (Rizk, 1987). Rubber has also been isolated from many *Euphorbia* species (Rizk, 1987).

Sesquiterpenes. Although several have been reported from the family, this class of compounds does not seem to be well represented (Ramaiah et al., 1979; Rizk, 1987).

Picrotoxins, a complex type of sesquiterpene, are found in the Menispermaceae (*Menispermum*, *Anamirta*, and *Cocculus*), the Coriariaceae, Orchidaceae (*Dendrobium*), and the Euphorbiaceae (*Hyaenanche*, Oldfieldioideae: Hyaenancheae) [e.g., pretoxin (88)] (Cane, 1981; Coscia, 1969). Mellitoxin is known to occur in *Hyaenanche globosa* Lamb. (Coscia, 1969).

Other compounds. A series of compounds including crotepoxide (89) is thought to be derived from *iso*-chorismic acid. This compound is found in *Croton macrostachys* Hochst. A series of α -glucosidase inhibitors, including α -homonojirimycin (90), has been described from *Omphalea diandra* L. (Euphorbioideae). These compounds resemble compounds found in legumes, the Moraceae, and the Polygonaceae and have promise as antitumor and antidiabetic drugs (Kite et al., 1988).

SYSTEMATIC VALUE OF CHEMICAL CHARACTERS

The chemistry of the Euphorbiaceae is among the most diverse of all plant families. As mentioned above, many of the most unusual classes of compounds are found only in this family and, hence, represent autapomorphic characters. Many others are of relatively simple biosynthetic origin and are widespread among higher plants.

Although the chemistry of most members of the family has been inadequately studied, our present knowledge of the chemistry of this family is becoming clearer and patterns are emerging. Undoubtedly, some surprises await additional phytochemical investigation.

Triterpenes are widespread in the Euphorbiaceae and are found in all five subfamilies. They are major components of the latex of the Crotonoideae and Euphorbioideae. Cucurbitacins (derived from triterpenes) are found in the Phyllanthoideae, Acalyphoideae, and Euphorbioideae.

Among the alkaloids, securinine alkaloids unite several genera of the Phyllanthoideae, and a series of nicotinic acid derived alkaloids, cyanogens, and 3-pyridones unite several genera of the Acalyphoideae.

The cyanogens of the Phyllanthoideae are all tyrosine derived, that of the Acalyphoideae nicotinic acid derived, and the cyanogens of the Crotonoideae are valine/isoleucine derived.

Kaurene derived diterpenes are found in the Crotonoideae and Oldfieldioideae. Monocyclic derived diterpenes are found in the Acalyphoideae, Crotonoideae, and Euphorbioideae. Cocarcinogenic diterpenes derived from these precursors are found commonly in the Euphorbioideae and Crotonoideae. Highly oxygenated diterpenes based on a labdane skeleton are found in the Crotonoideae and Acalyphoideae.

In summary, several chemical features serve to link the five subfamilies. The Oldfieldioideae have been insufficiently studied.

There are few chemical similarities between the Flacourtiaceae and the Euphorbiaceae (Hegnauer, 1989).

Many species of the genera *Buxus*, *Pachysandra*, and *Sarcococca* possess unusual steroidal and triterpenoid alkaloids. These compounds are found only in the Buxaceae and are distinct from those of euphorbiaceous plants (some are similar to the alkaloids of plants in the Apocynaceae). A number of relatively common triterpenes found in the genus *Buxus* also occur in the Euphorbiaceae (Hegnauer, 1989). Although *Simmondsia* is sometimes considered to be a member of the Euphorbiaceae, these

plants lack the alkaloids characteristic of the Buxaceae and Euphorbiaceae and have unusual nitriles not found in either family (Hegnauer, 1989).

The triterpene alkaloids of the Daphniphyllaceae are unique and do not resemble those of the Euphorbiaceae (Hegnauer, 1989; Rizk, 1987). There is no significant chemical similarity between this family and the Euphorbiaceae.

The Celastraceae and Rhamnaceae both have peptide and maytansanoid alkaloids similar to those of several genera of Euphorbiaceae (Hegnauer, 1989). Benzylisoquinoline alkaloids also are known from the Rhamnaceae (*Rhamnus*, *Phyllica*, *Colletia*, *Colubrina*, *Discaria*, *Ratanilla*, *Talguenea*, and *Zizyphus*) as well as from the Euphorbiaceae (primarily the genus *Croton*). Many relatively common types of triterpenes are found in these families along with certain oxidatively altered ones. The spectrum of other compounds in the Celastraceae and Rhamnaceae (including sesquiterpene and spermine alkaloids, anthraquinone and naphthaquinone pigments, seed lipids, and cardiac glycosides) is not particularly similar to those of euphorbiaceous plants.

Some unusual lipids occur in seeds of the Malvaceae, Sterculiaceae, and Bombacaceae; cyclopropenoid fatty acids are especially common (Hegnauer, 1989; Smith, 1970). Peptide alkaloids are found in the Sterculiaceae (*Melochia* and *Waltheria*) as well as in euphorbiaceous genera. Overall, the chemistry of plants typically placed in the Malvales (Malvaceae, Sterculiaceae, Bombacaceae, Tiliaceae, Elaeocarpaceae, etc.) shows some similarity, but does not strongly resemble that of the Euphorbiaceae.

The chemistry of members of the Geraniales (Geraniaceae, Oxalidaceae, Limnanthaceae, Tropaeolaceae, Balsaminaceae, Linaceae, Erythroxylaceae, Humiriaceae, Zygophyllaceae, Malpighiaceae, Trigoniaceae, Polygalaceae, Krameriaceae, Vochysiaceae, etc.) does not greatly resemble that of the Euphorbiaceae. The Limnanthaceae and Tropaeolaceae contain glucosinolates, as does the euphorbiaceous genus *Drypetes* (and *Putranjiva*, if not included in *Drypetes*). Several species of the genus *Linum* are cyanogenic and contain the cyanogenic compounds linamarin, lotaustralin, linustatin, and neolinustatin, as do some members of the Crotonoideae. However, linamarin and lotaustralin are the most widespread of all cyanogenic compounds among higher plants. Many species of the Geraniaceae accumulate monoterpenes. The floral lipids of the Malpighiaceae and Krameriaceae contain unusual fatty acid and glyceride mixtures, but these are not found in the Euphorbiaceae (al-

though equally unusual floral lipids are found in species of *Dalechampia*). The tropane alkaloids of coca are found in *Erythroxylum* (Erythroxylaceae), and also in other families, especially the Solanaceae (Seigler, 1977).

The Thymelaeaceae have the strongest chemical link to the Euphorbiaceae. Because of the complex and lengthy biosynthetic pathways leading to the formation of cocarcinogenic diterpenes and their highly restricted distribution (only in the Euphorbiaceae and Thymelaeaceae), it seems highly probable that the families are closely related. This relationship has been observed on a basis of more classical characters as well; both Dahlgren et al. (1981) and Thorne (1981) placed the Euphorbiaceae and Thymelaeaceae close together in their respective phylogenetic systems. Other strong chemical similarities between the two families are not yet fully understood; the chemistry of plants of the Thymelaeaceae has not been thoroughly studied.

Perhaps the chemical data speak best for the situation described by Webster (1987), in which the Euphorbiaceae are derived from some group intermediate to the Geraniales and Malvales. It seems likely that the chasm between the Dilleniidae and Rosidae (Cronquist, 1981) has been exaggerated. The Thymelaeaceae probably are closely related to the Euphorbiaceae, although, perhaps, they should be placed in a parallel but distinct order. Other affinities are suggested with the Rhamnaceae and Celastraceae.

Although chemical data are helpful in understanding the affinities of this most enigmatic family, the final resolution of the phylogenetic placement of the Euphorbiaceae remains a goal to be determined through future research based on a combination of molecular, phytochemical and morphological approaches.

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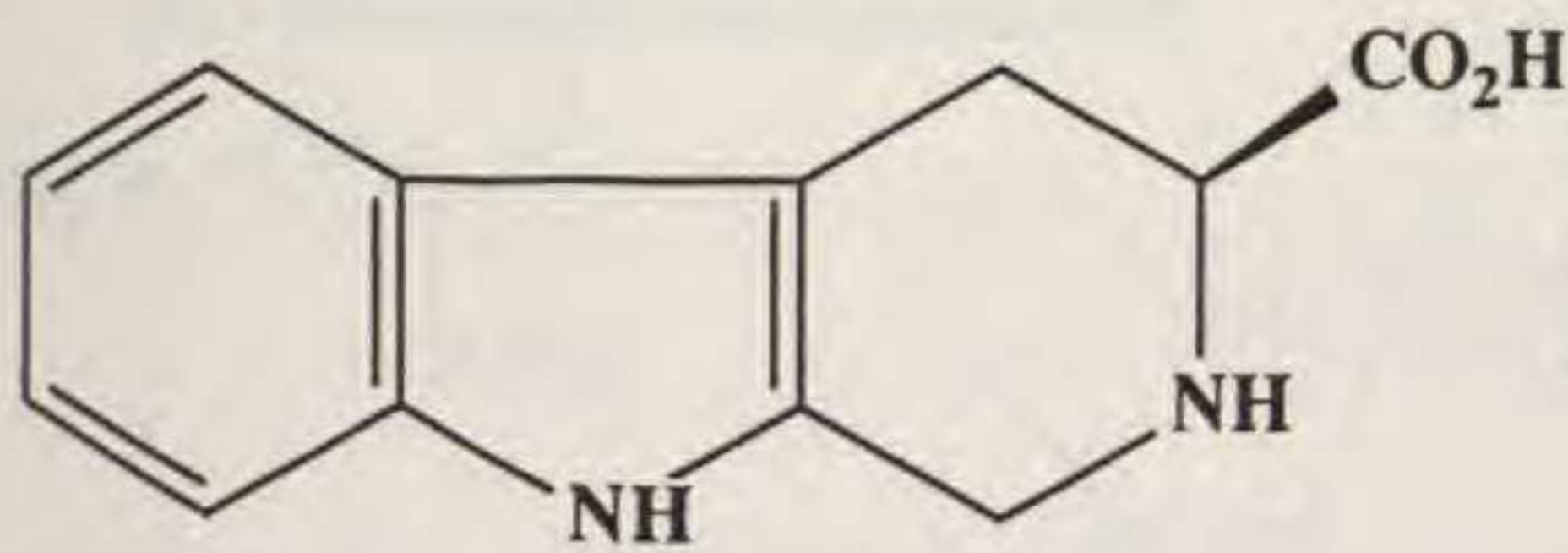
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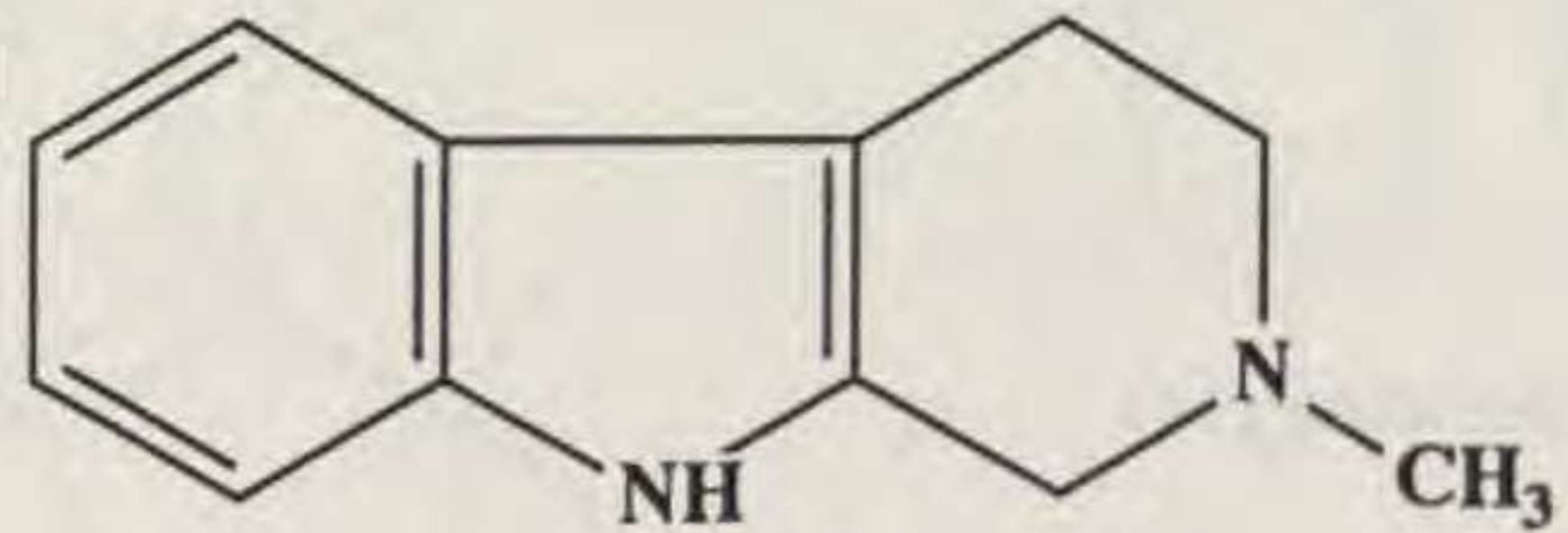
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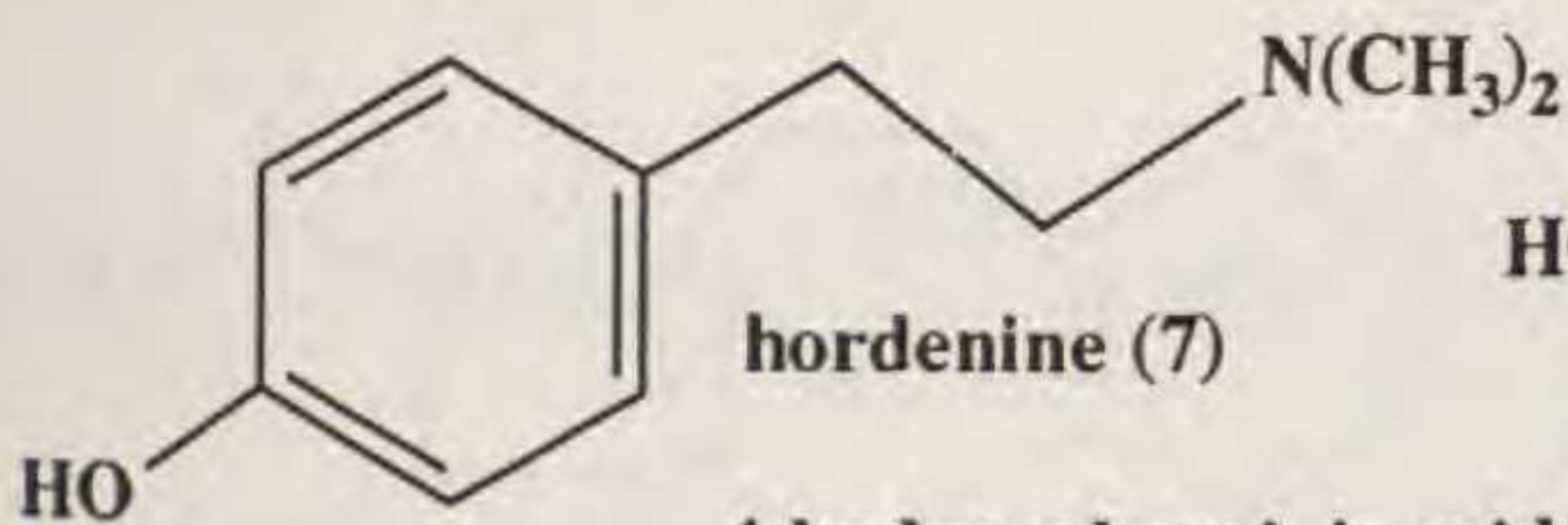
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L-3-carboxy-1,2,3,4-tetrahydrocarboline (1)

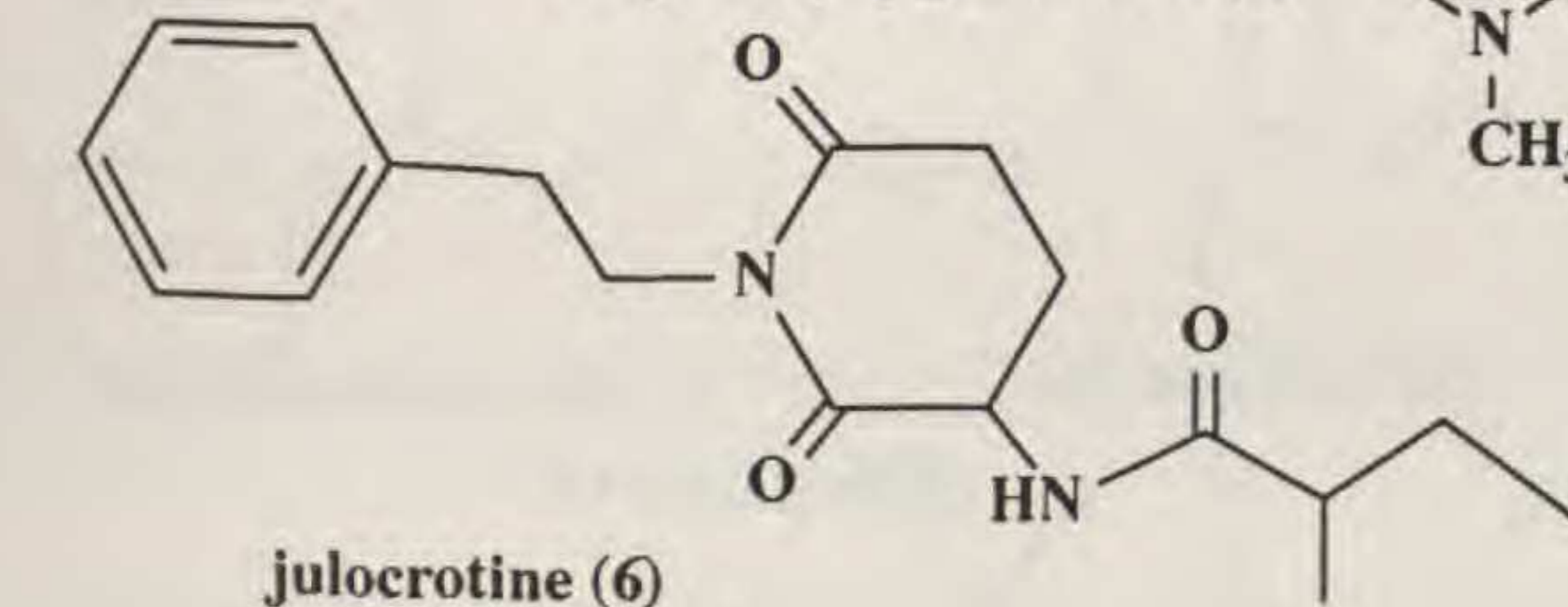
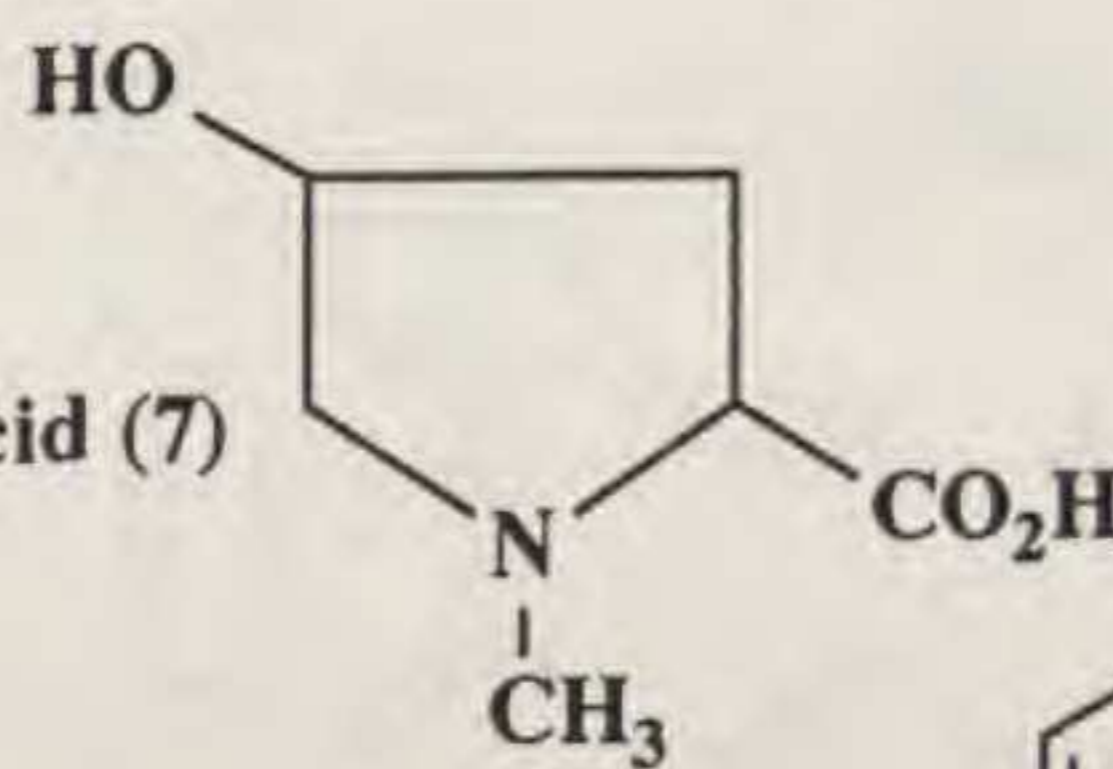


Nβ-methyltetrahydroharman (2)

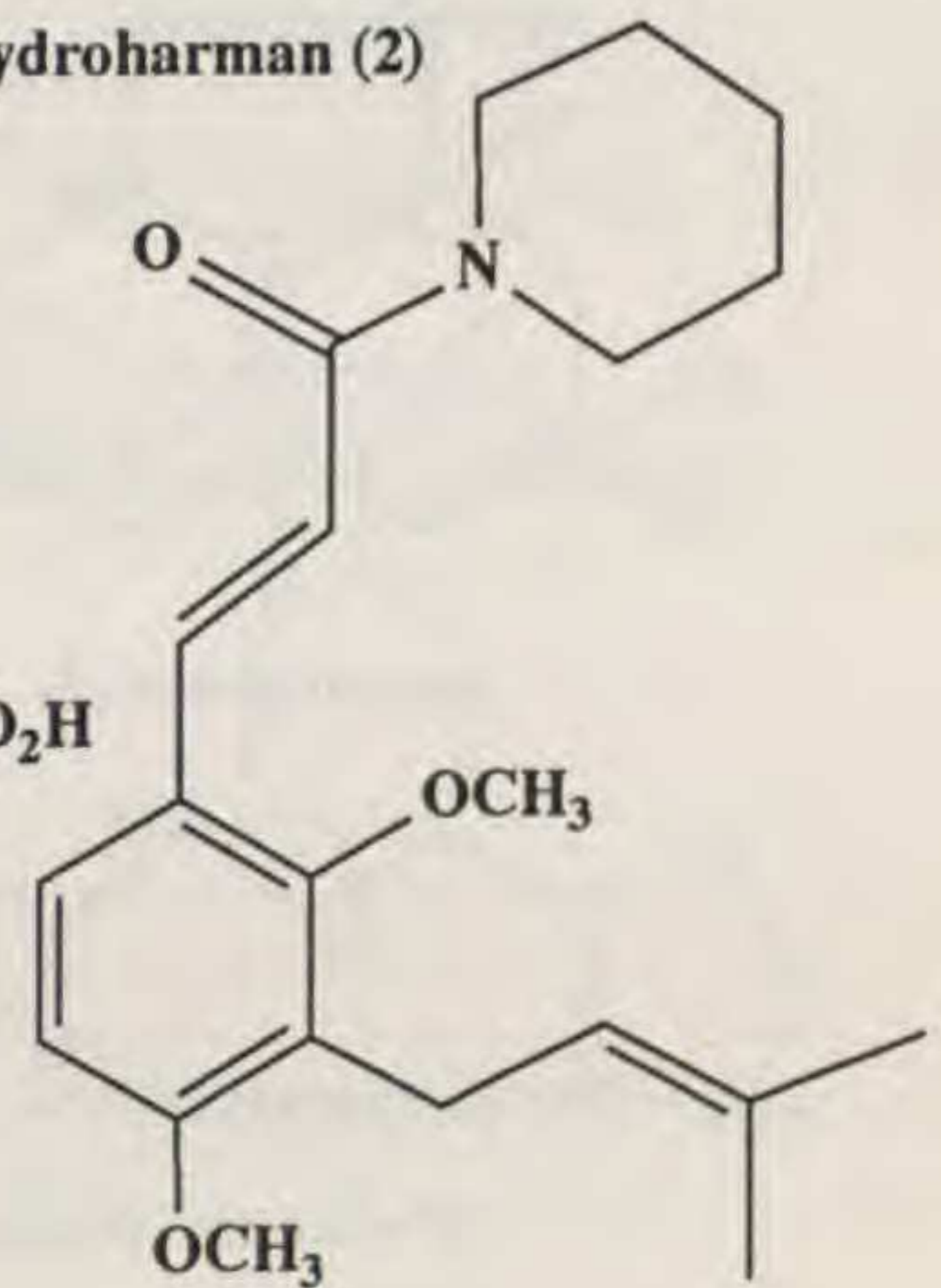


hordenine (7)

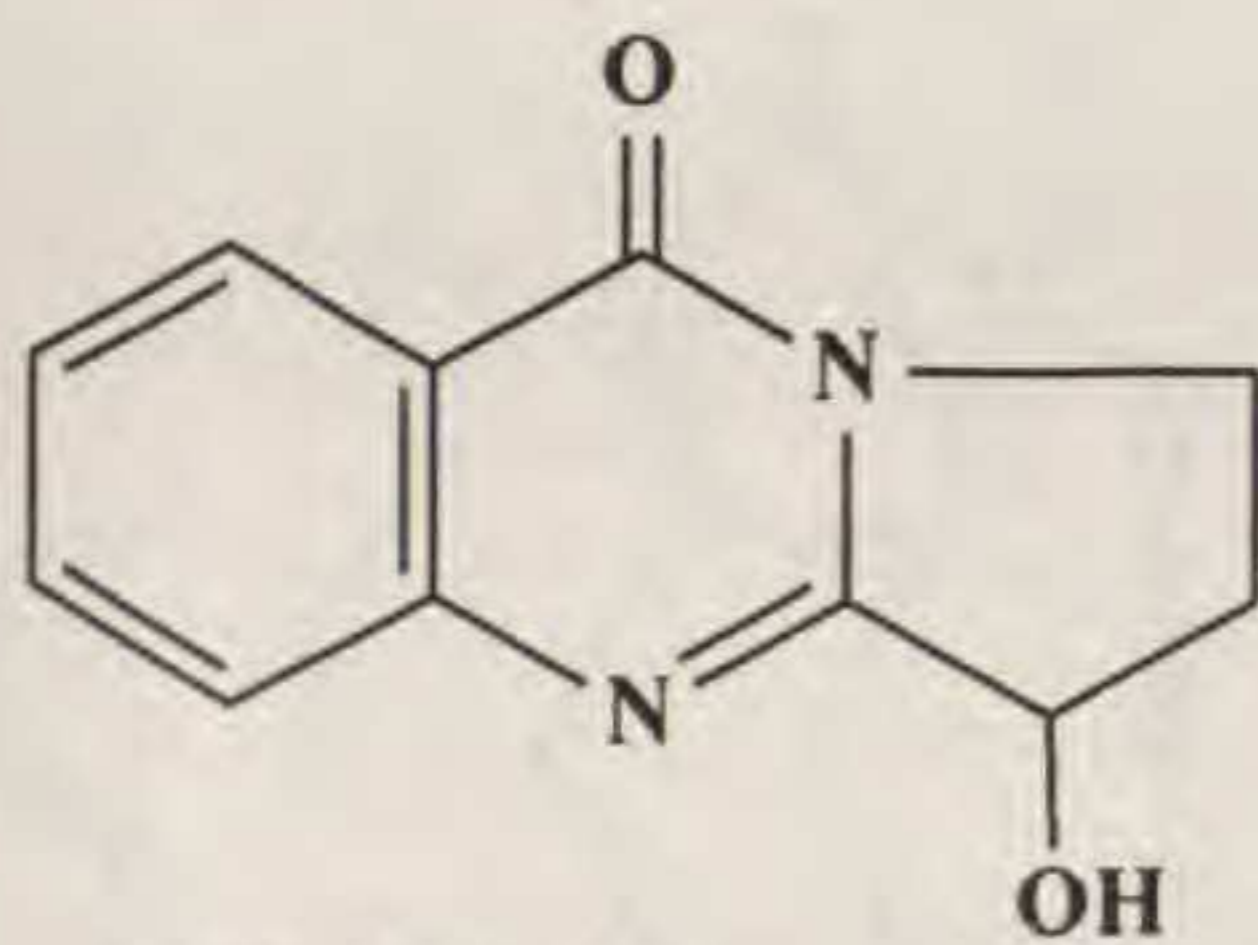
4-hydroxyhygrinic acid (7)



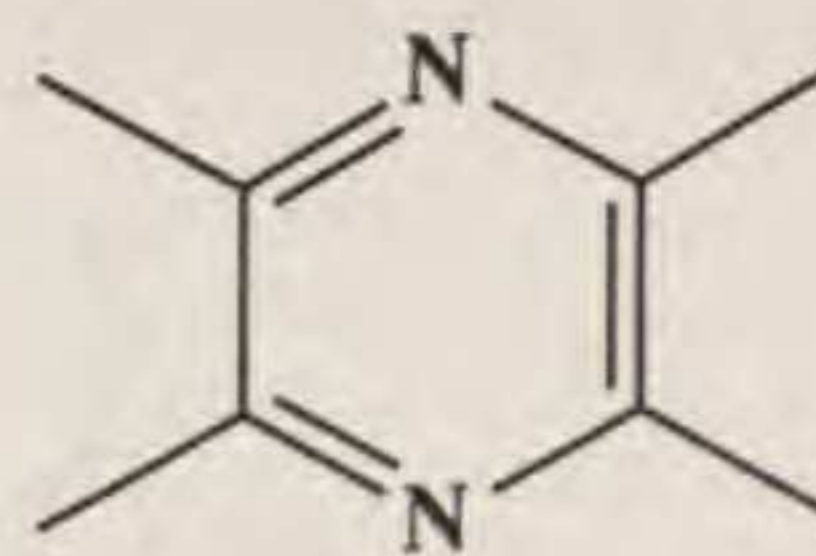
julocrotine (6)



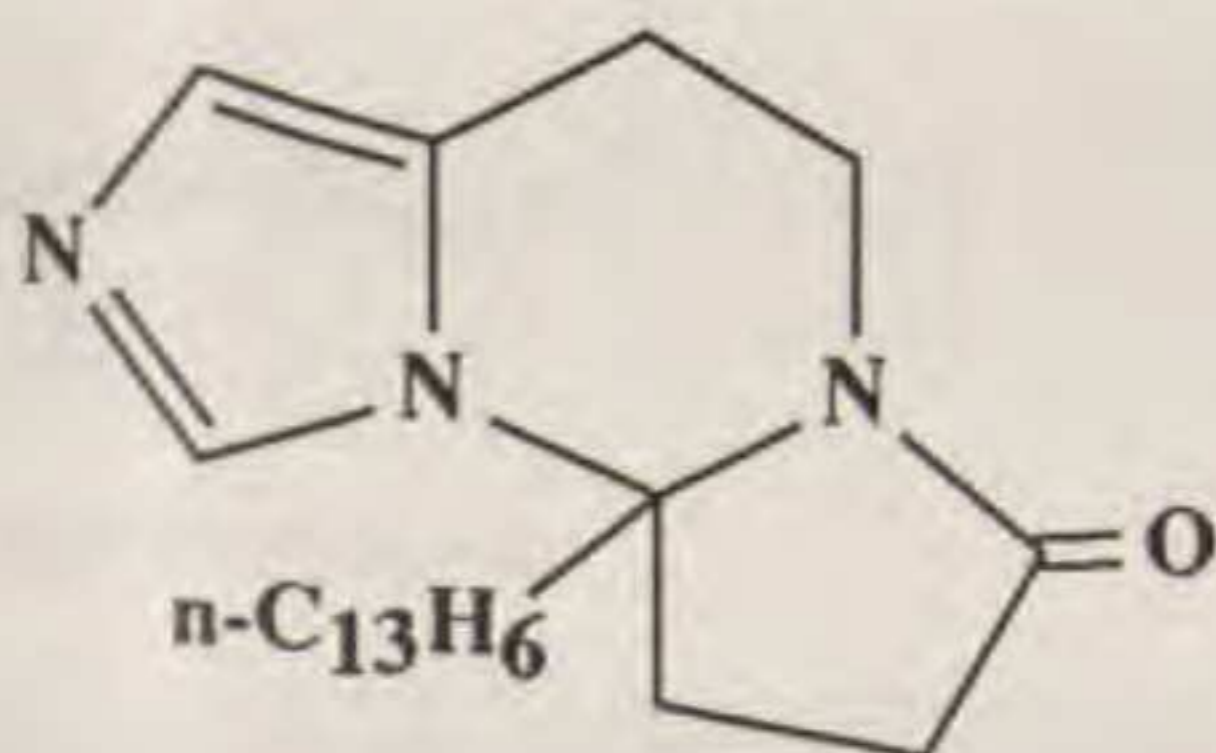
2,4-dimethoxy-Ψ,Ψ-dimethylallyl-E-cinnamoylpiperidide (5)



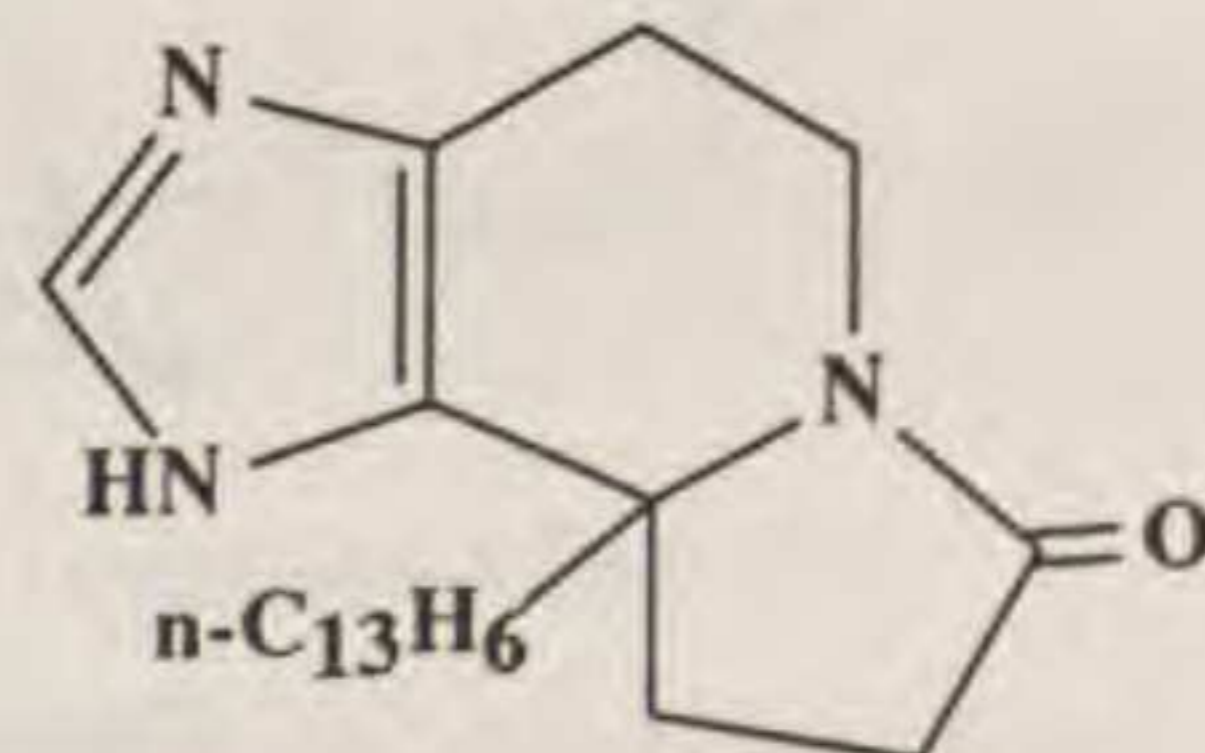
vasicine (3)



tetramethylpyrazine (9)



glochidine (12)



glochidine (11)

FIGURE. Chemical structures found in Euphorbiaceae grouped by chemical type. The number of each structure corresponds to the boldface number in parentheses following the chemical name in the text. Compounds number 1-29 and 31-32 are alkaloids, 30 and 33-37 are cyanogenic glycosides, 38-52 are diterpenes, 53-54 are glucosinolates, 55-67 are fatty acids, 68-70 are hydrolyzable tannins, 71-81 are triterpenes, 82 is an amine, 83 is a coumarin, 84-87 are flavonoids, 88 is a sesquiterpene, 89 are of other biosynthetic origin.

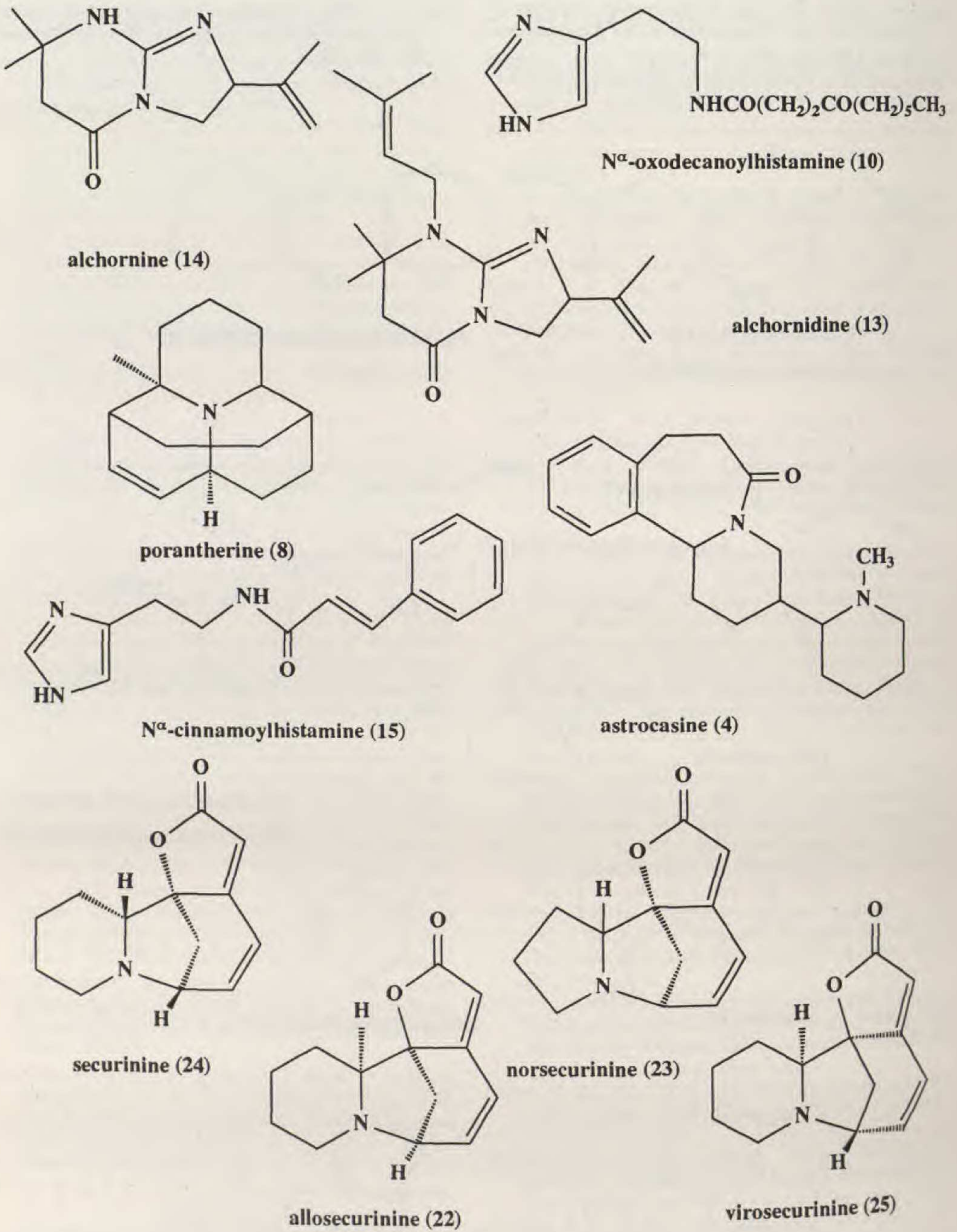
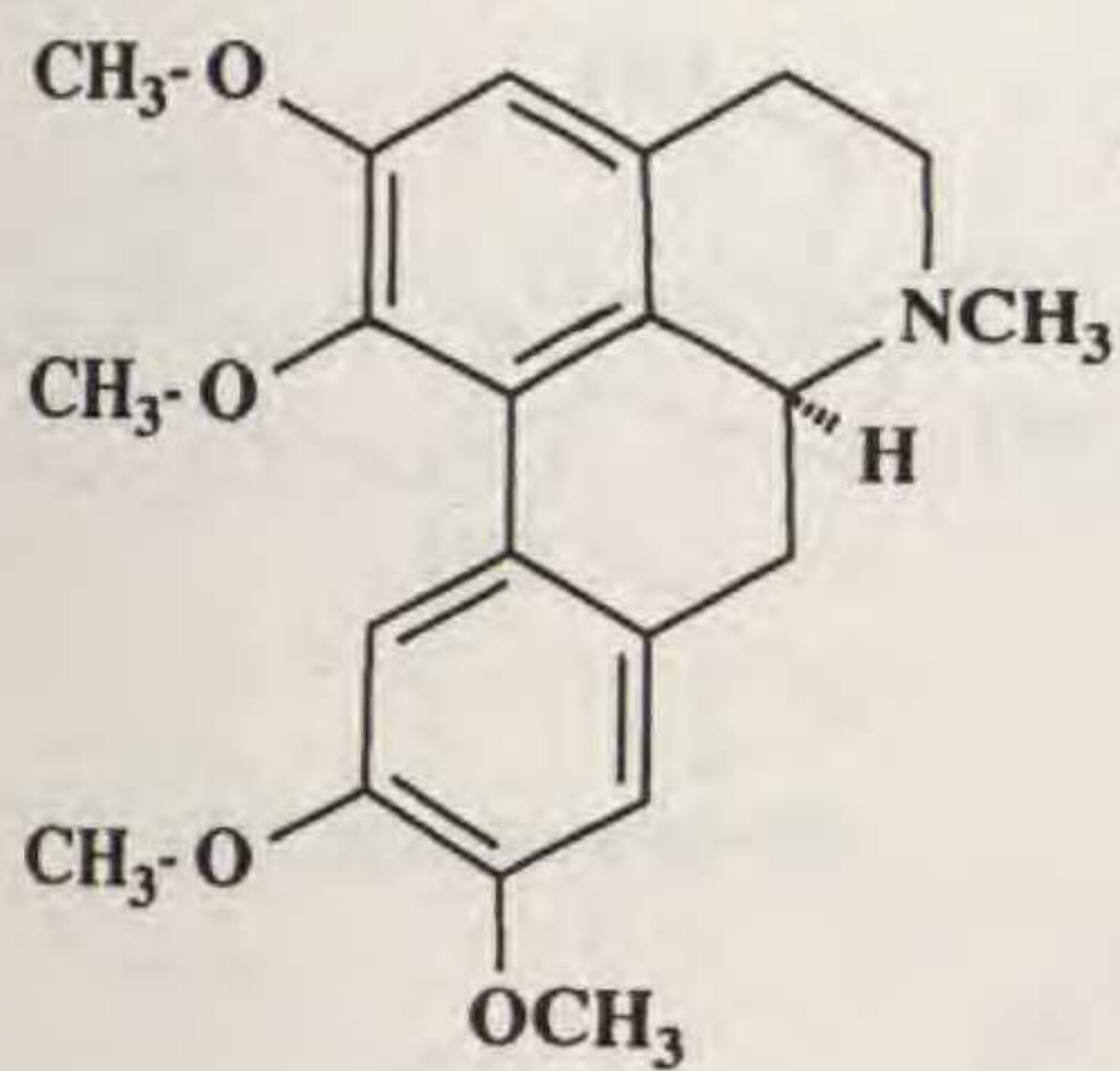
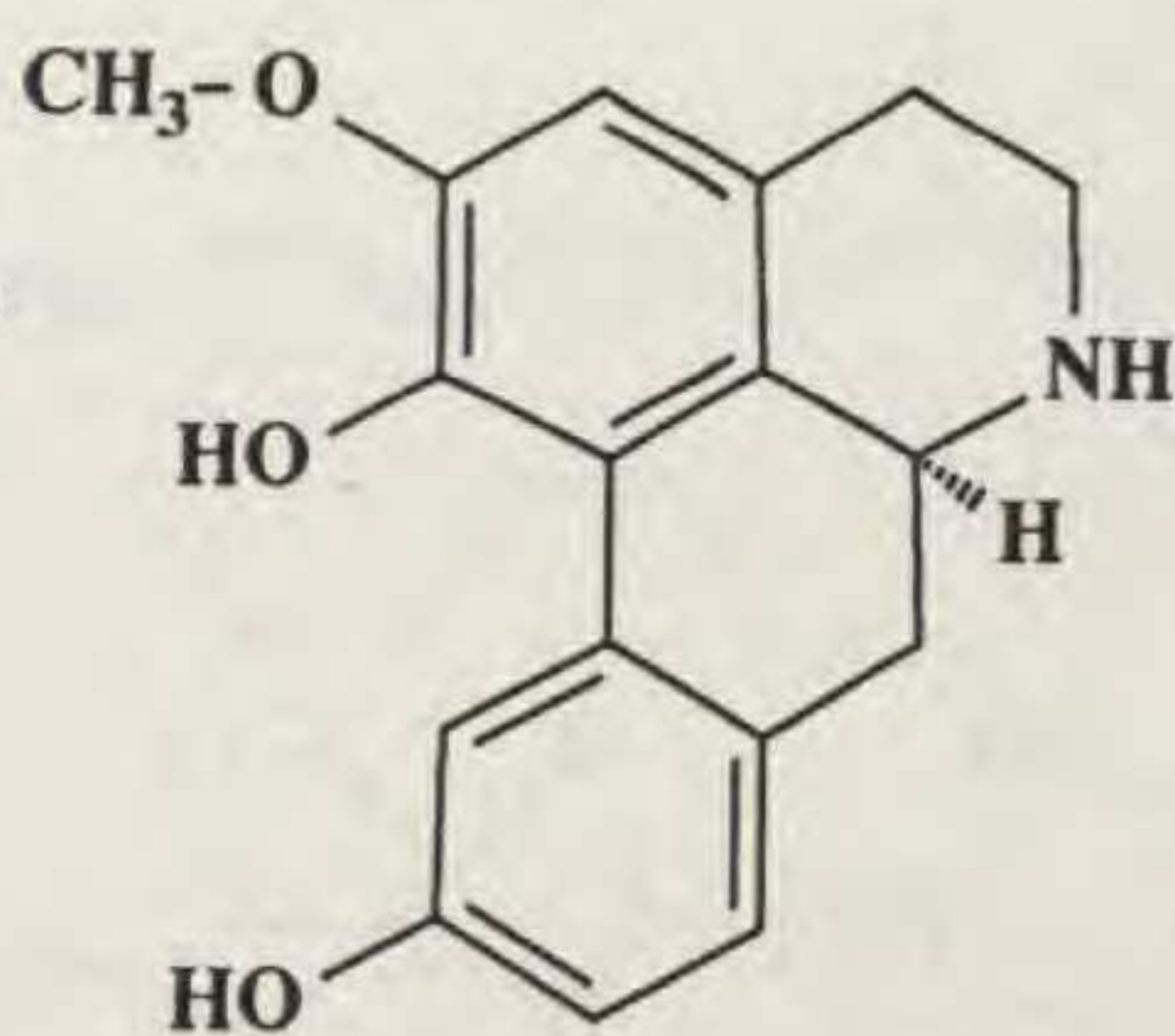


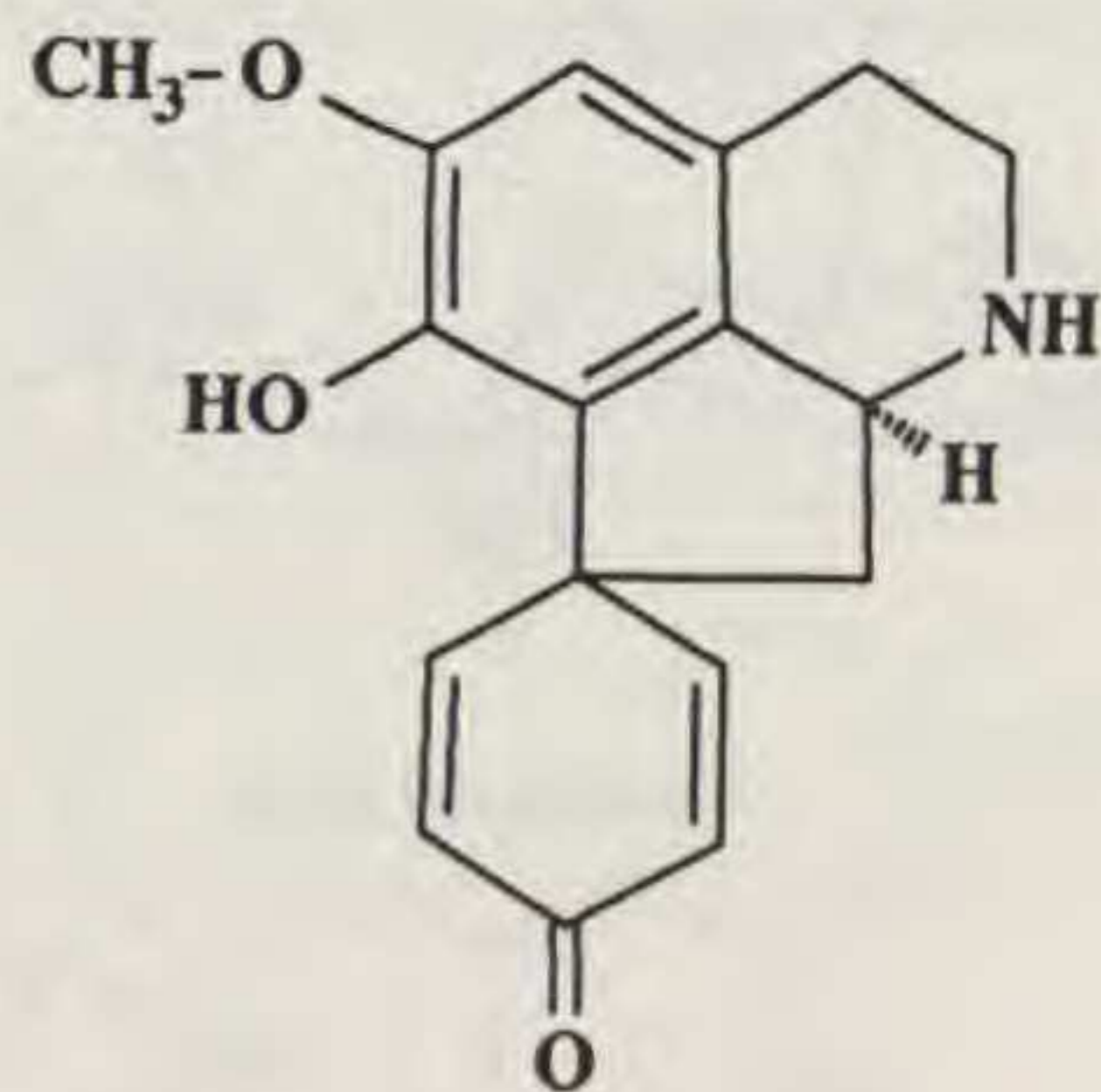
FIGURE. Continued.



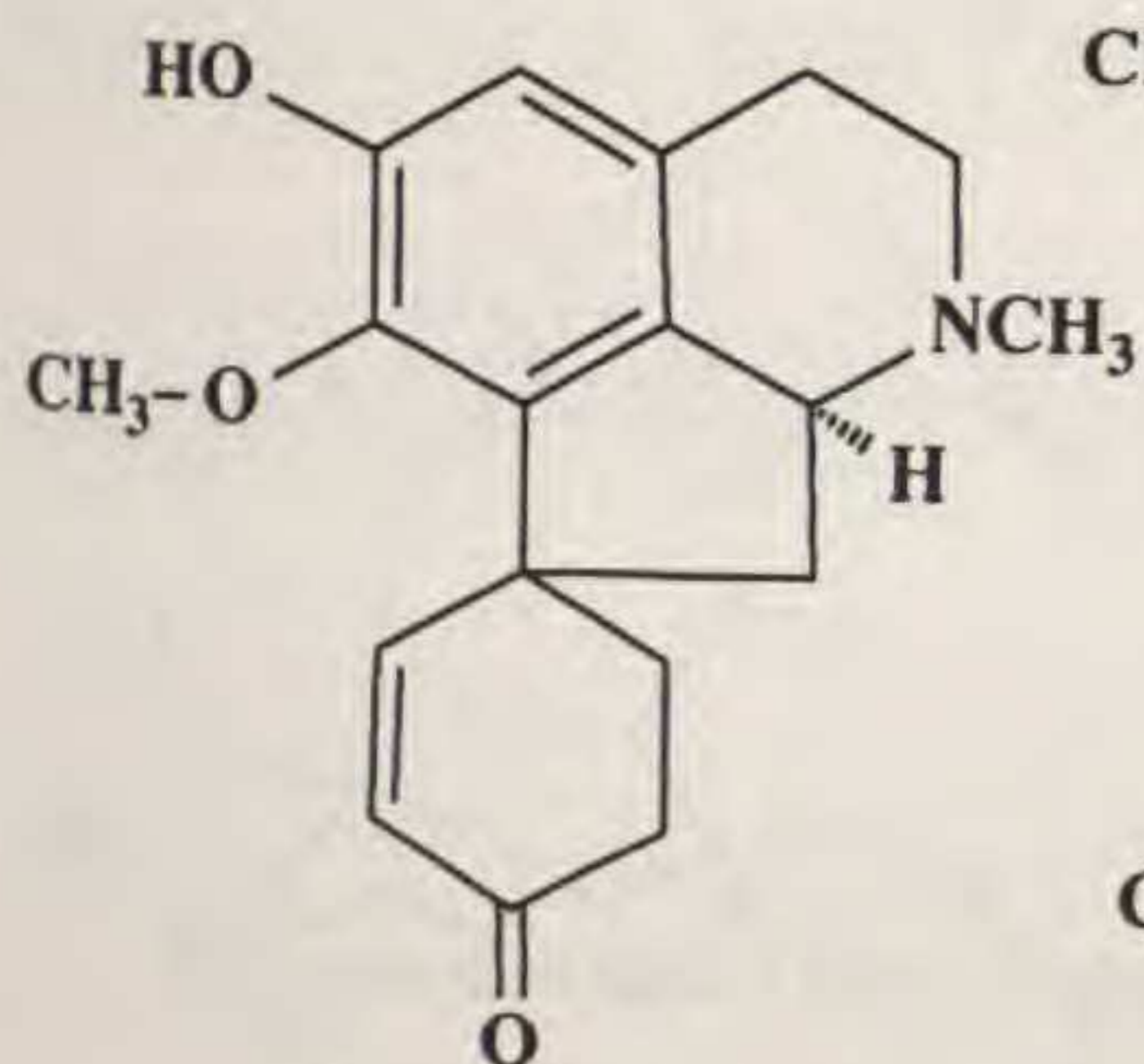
(+)-glaucine (16)



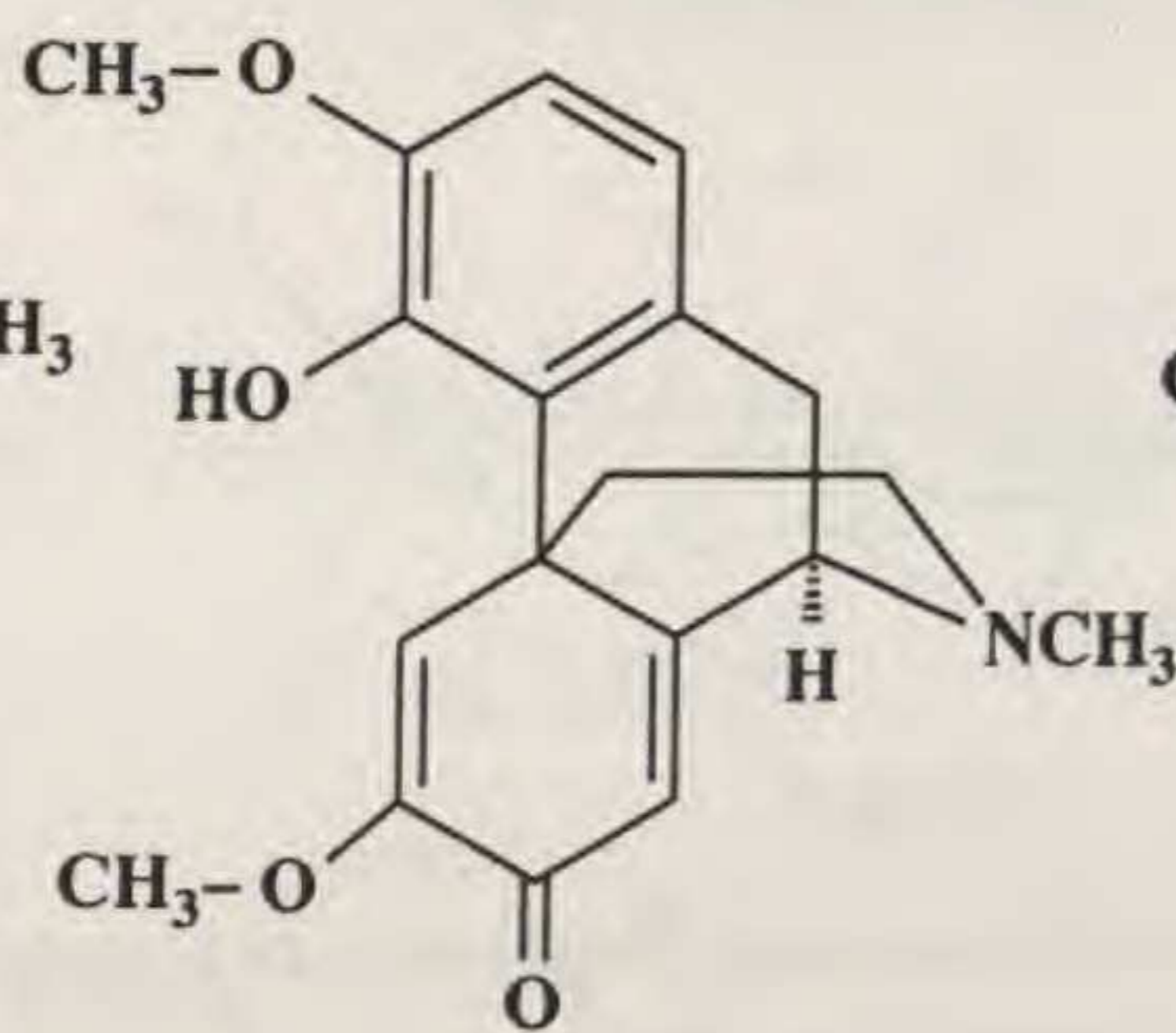
sparsiflorine (17)



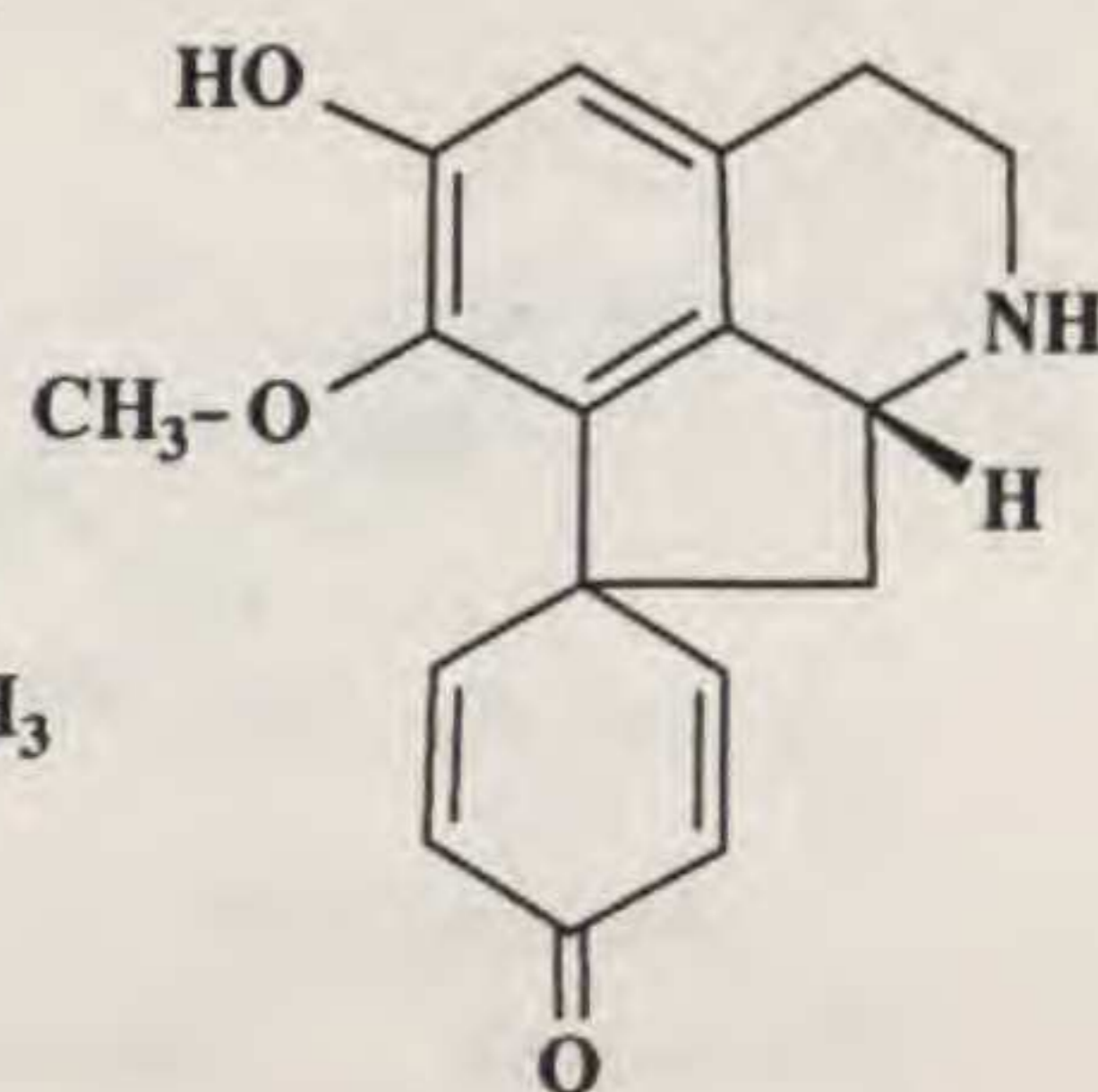
crotsparine (18)



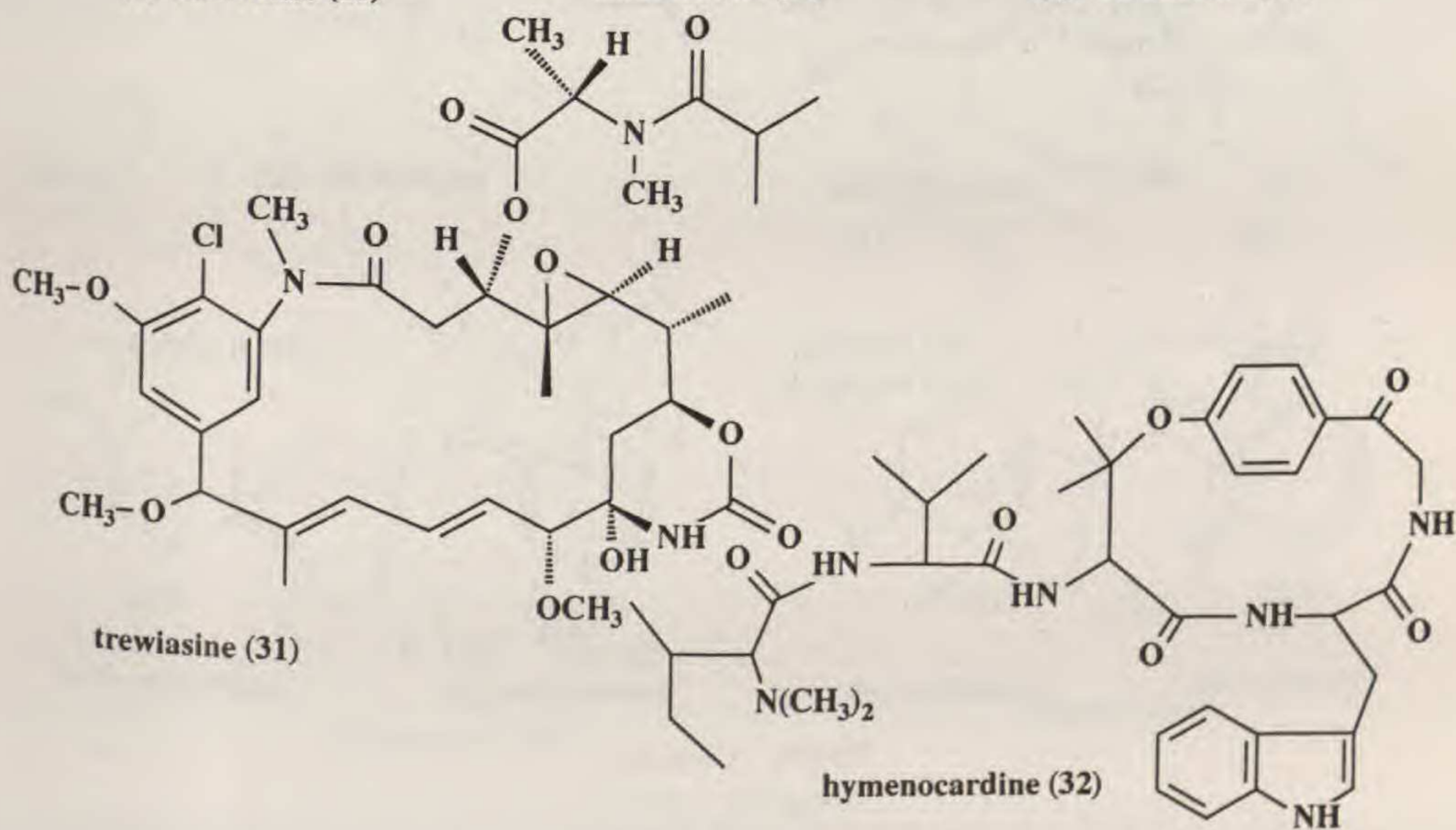
(+)-linearisine (20)



salutaridine (21)



(+)-crotonosine (19)



trewiasine (31)

hymenocardine (32)

FIGURE. Continued.

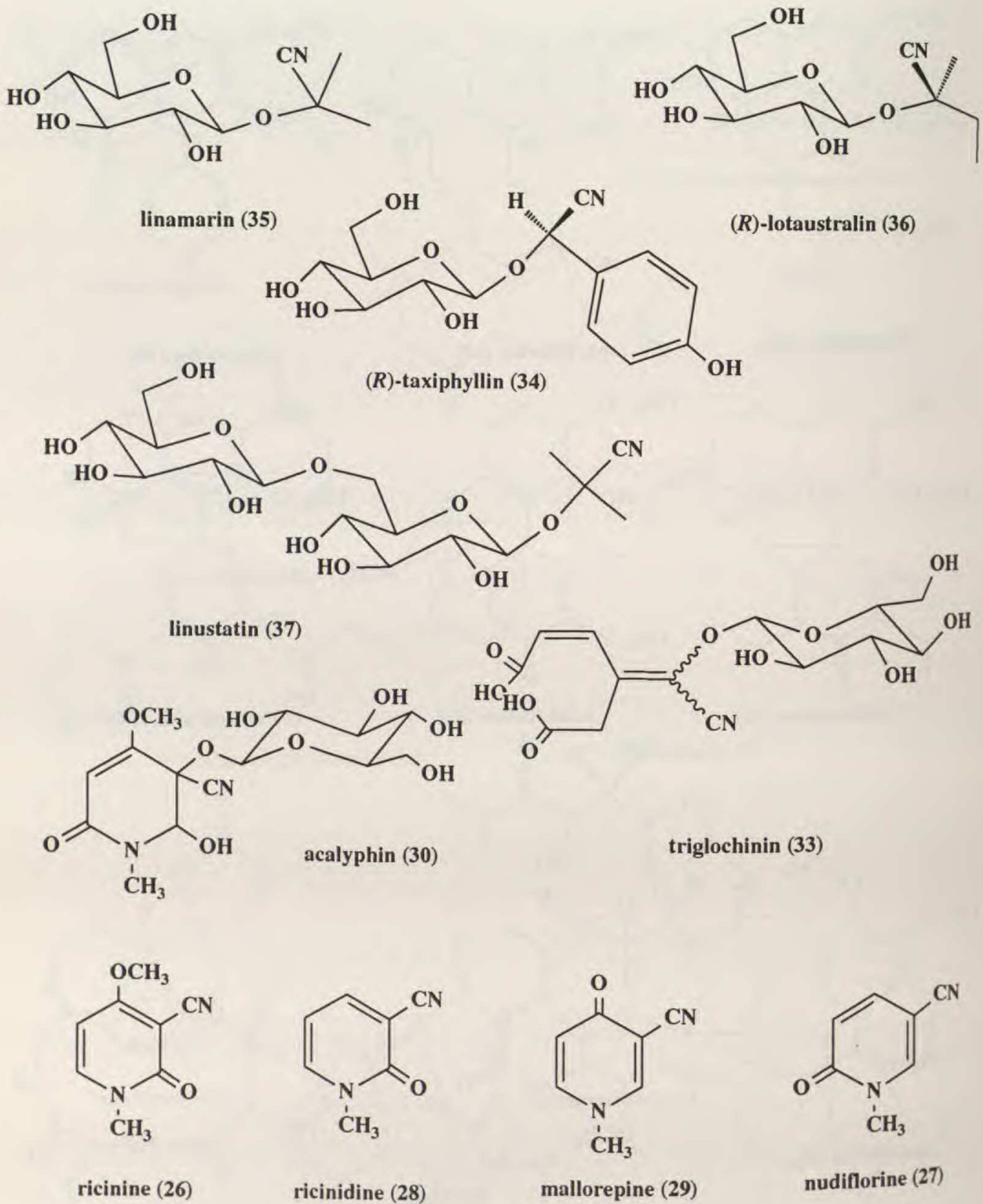


FIGURE. Continued.

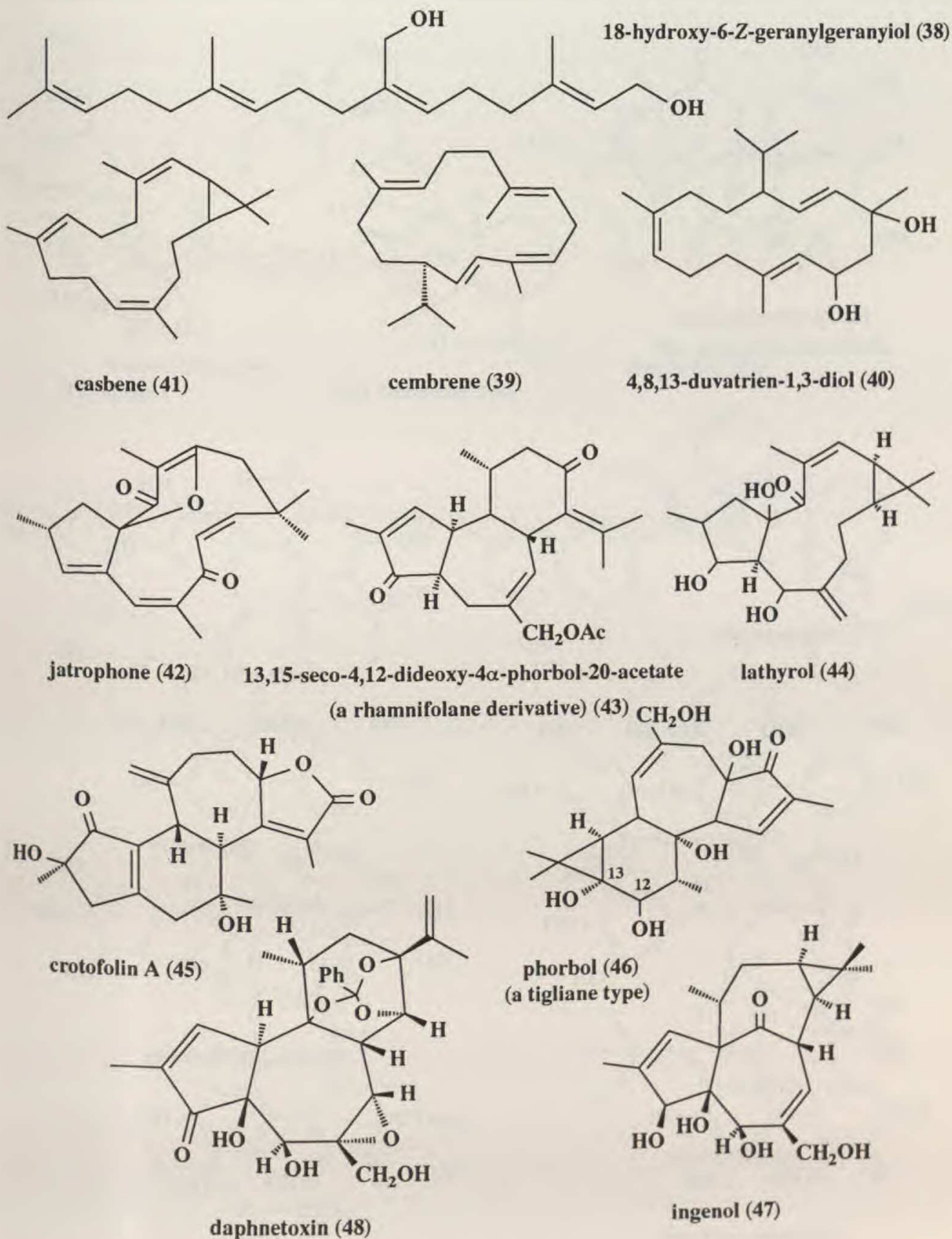
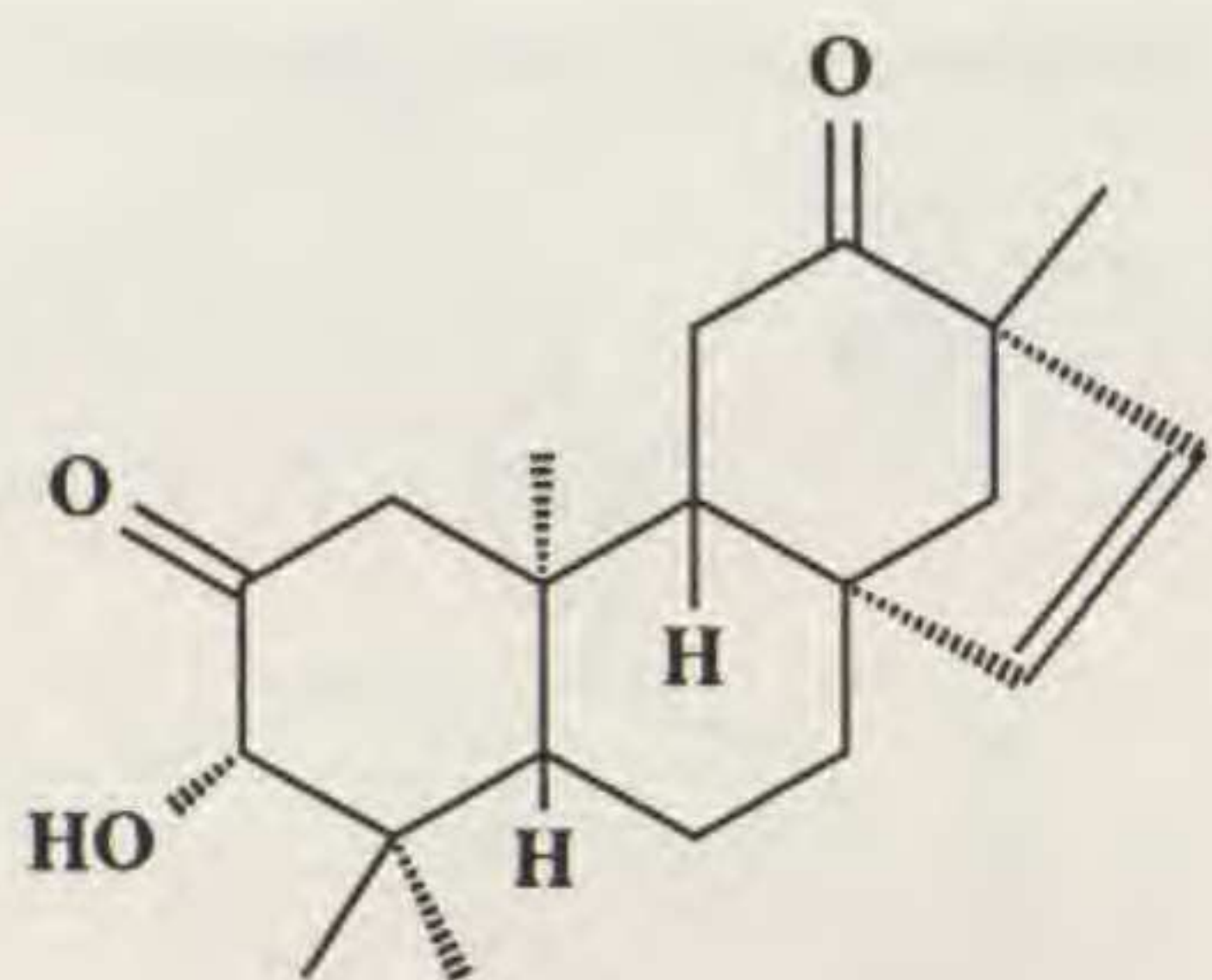
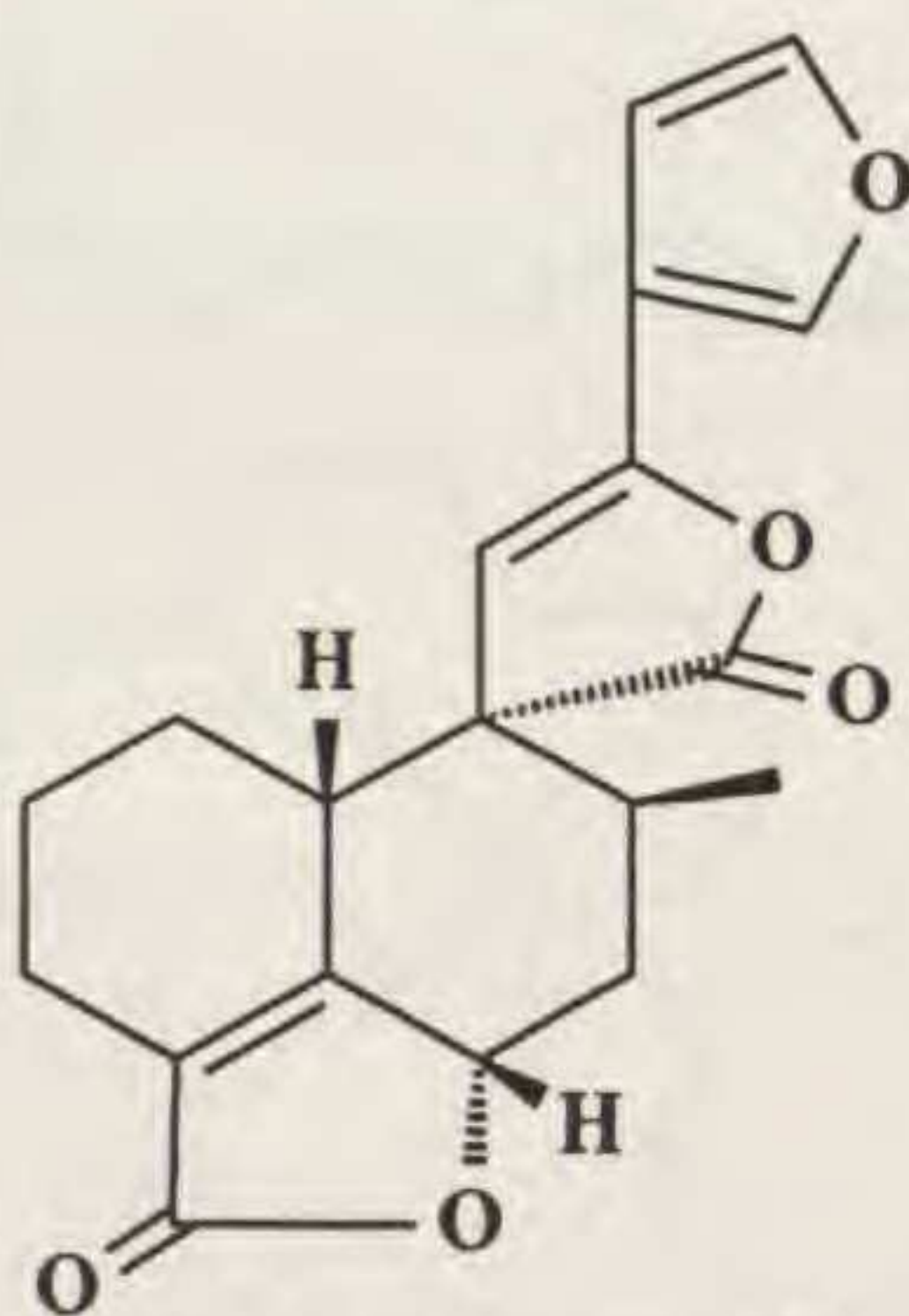


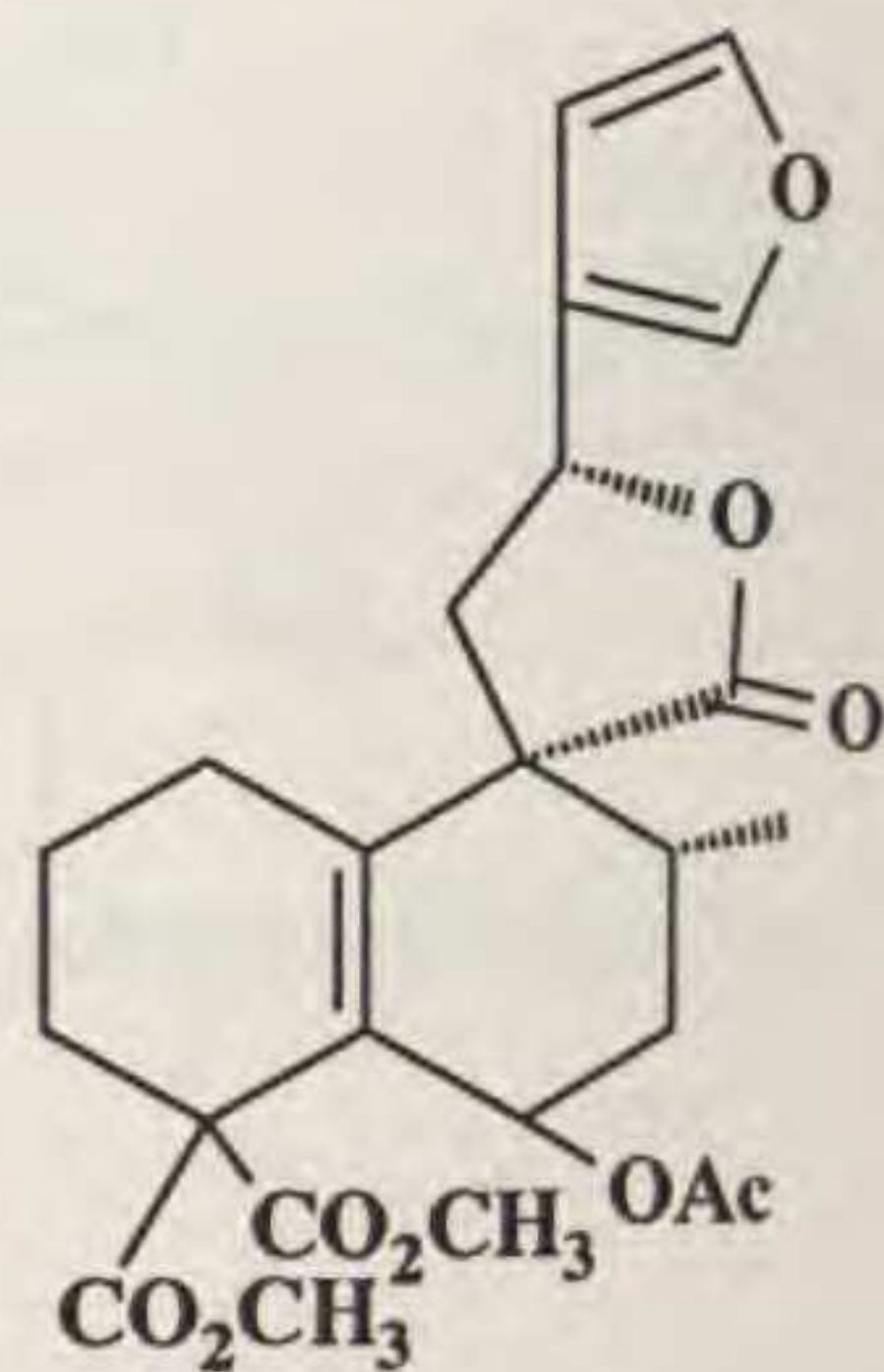
FIGURE. Continued.



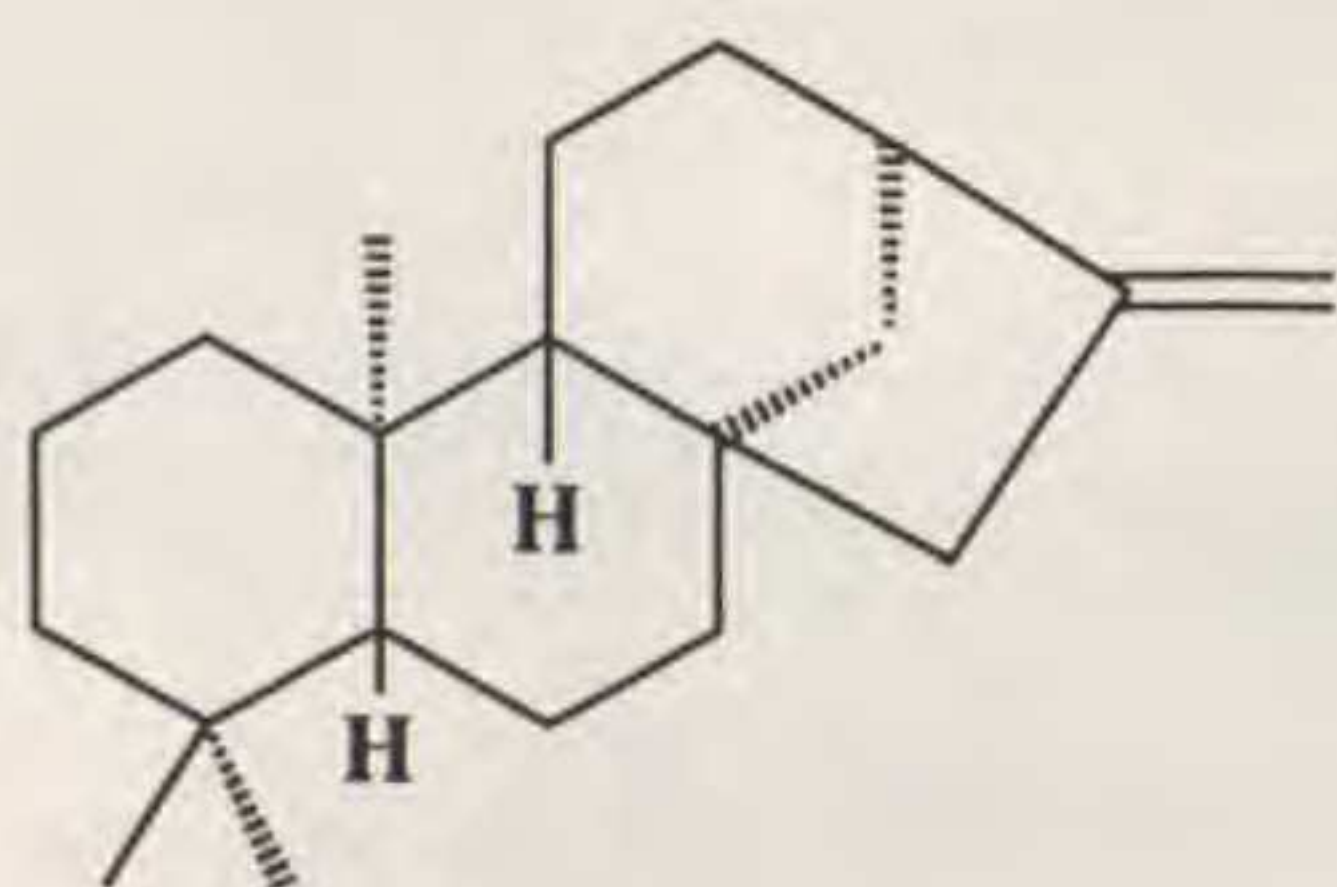
ent-3 β -hydroxybeyer-
15(16)-ene-2,12-dione (50)



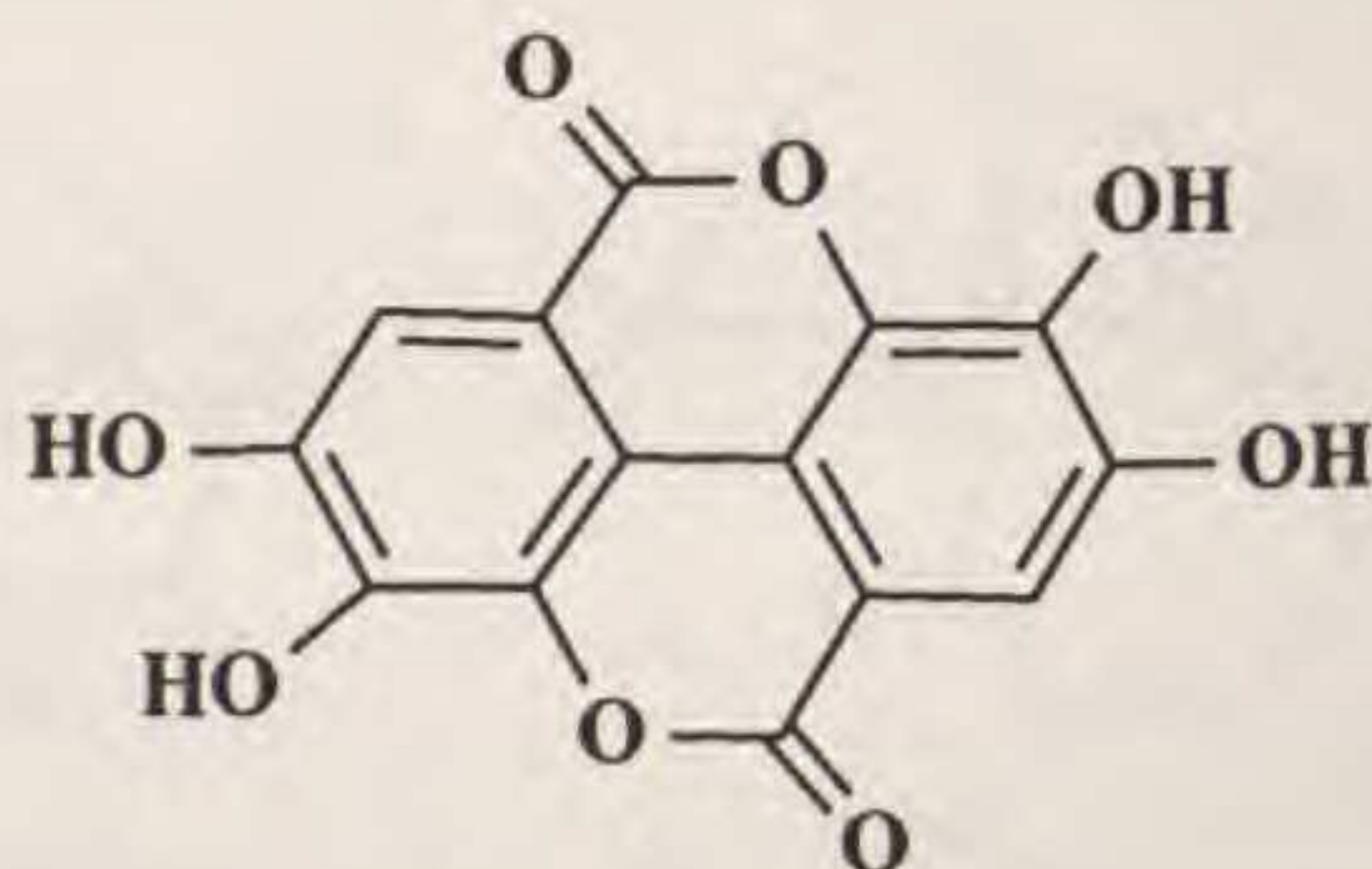
isocrotocaudin (51)



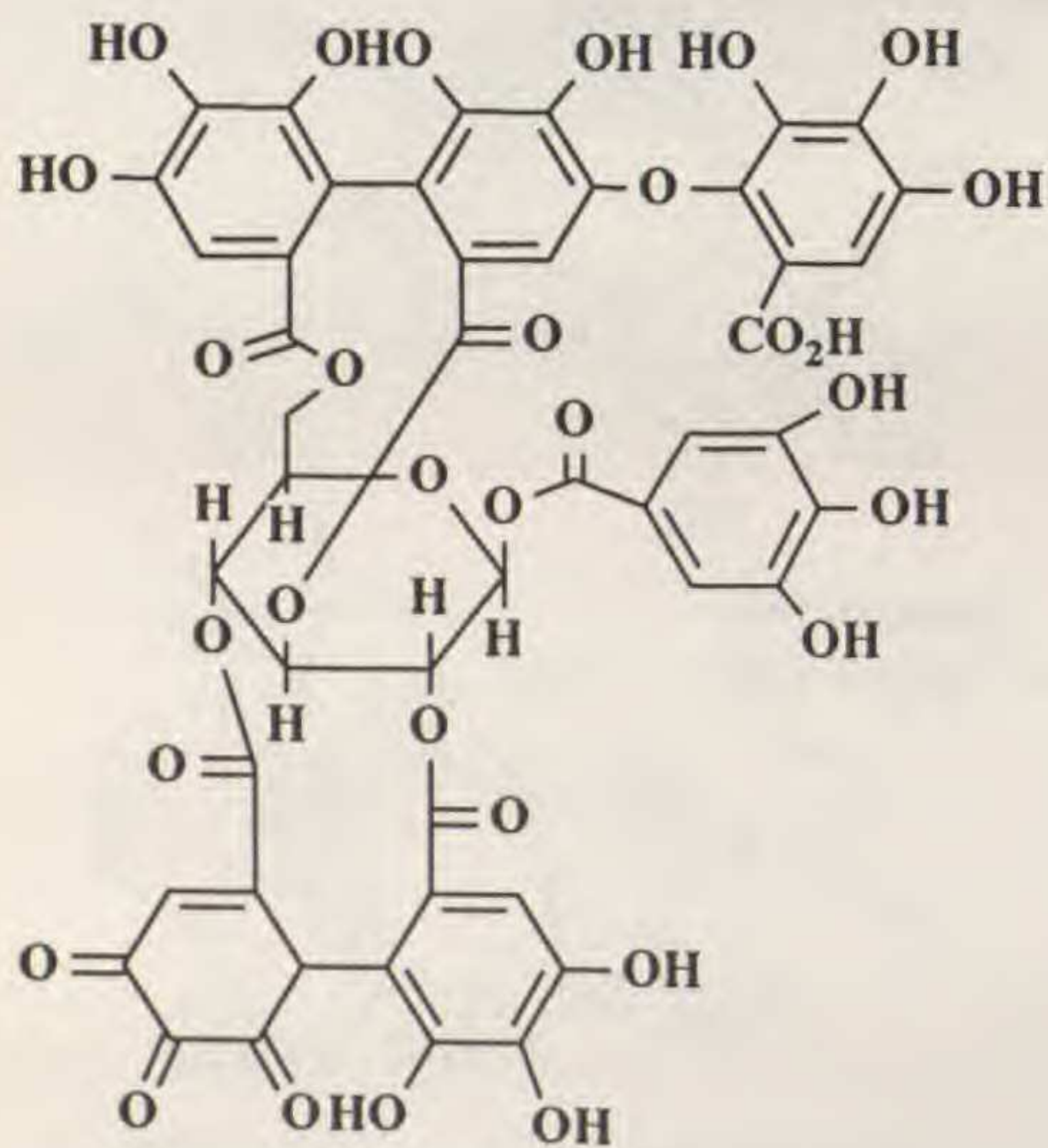
teucrin (52)



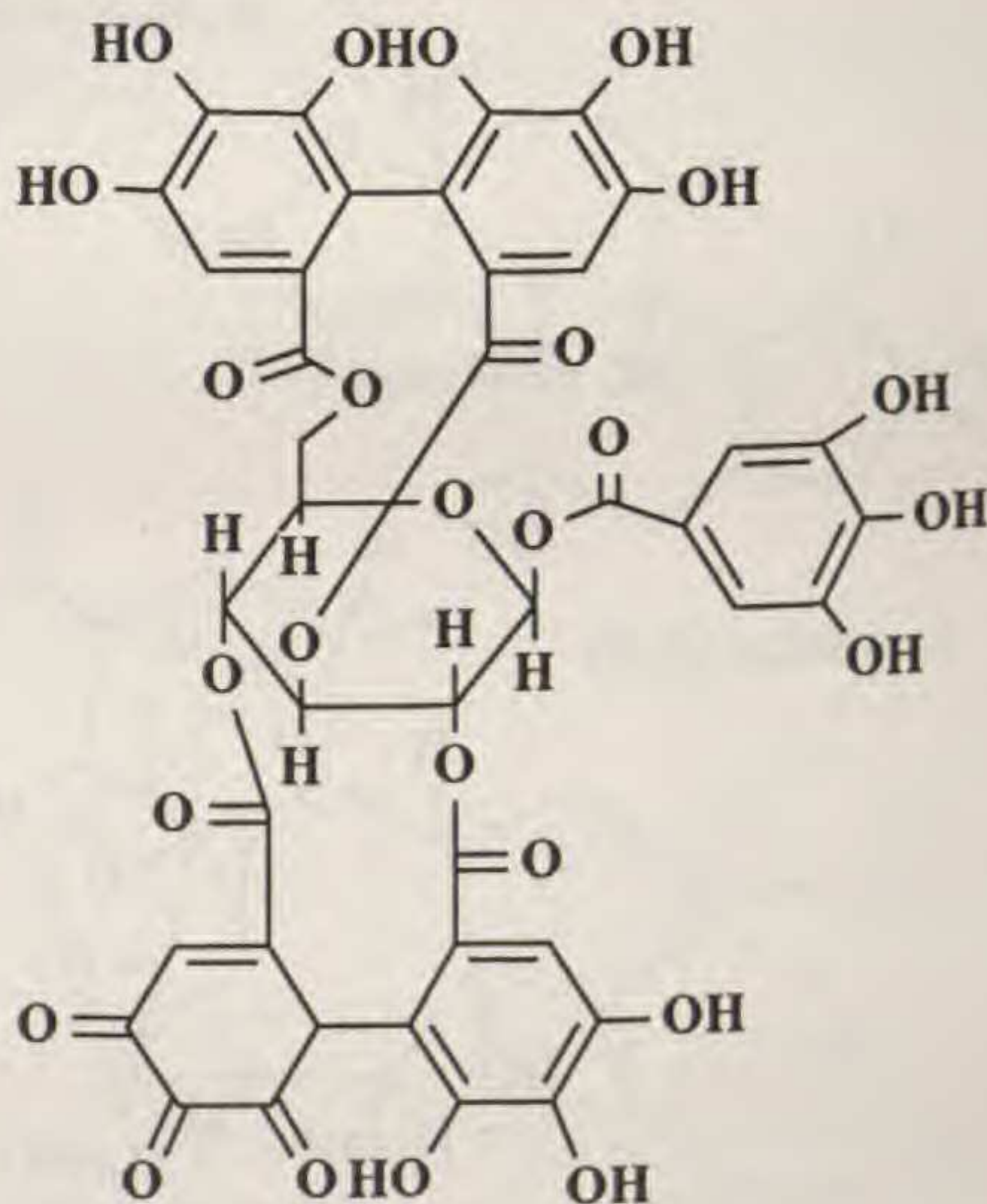
(-)-kaurene (49)



ellagic acid (68)



mallotusin acid (70)



geraniin (69)

FIGURE. Continued.

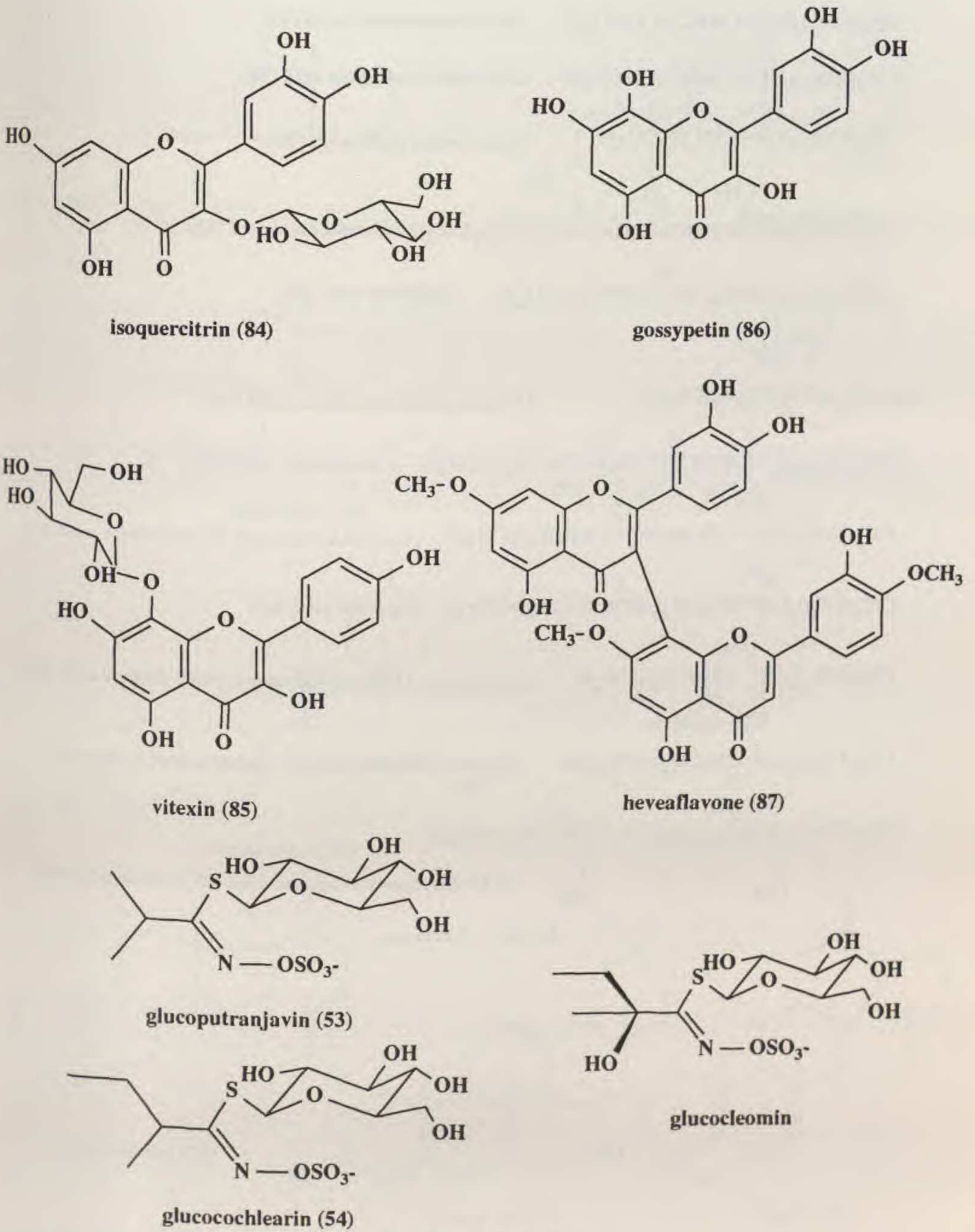


FIGURE. Continued.

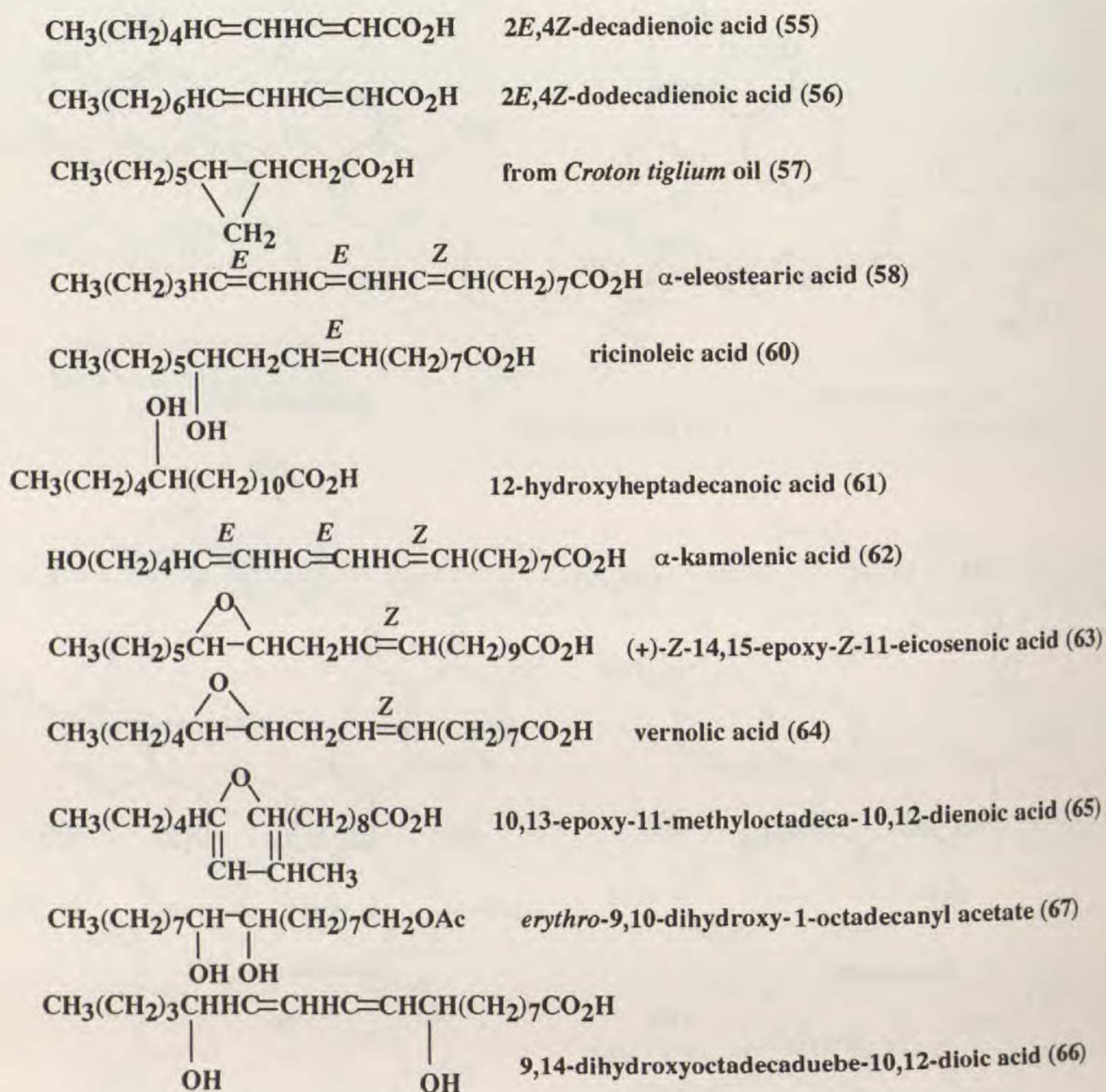


FIGURE. Continued.